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☐ 1. Document ID: US 5604108 A

L1: Entry 1 of 1 File: USPT Feb 18, 1997

US-PAT-NO: 5604108
DOCUMENT-IDENTIFIER: US 5604108 A

TITLE: Test for determining the dose response of a conjugated vaccine

Full | Title [redacted]

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Ryall-Robert.IN.	1

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Devi, S.
10/054638

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S2 352 S1 AND (TOXOID? ? OR TT OR DT OR OMP? ? OR OUTER(W)MEMBRAN-?(W)PROTEIN? ? OR CRM197 OR CRM(2W)197)
S3 67 S2 AND ((AL OR ALUMIN?)(W)(OH OR HYDROXIDE OR PHOSPHATE OR PO??) OR ALUM OR ALHYDROGEL? ? OR ALHYDRO(W)GEL? ? OR ALOH? ? OR ALPO??)

S7 31 S3/TI,DE,MAJ
S8 23 RD (unique items)
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8/3,AB/1 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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15563556 PASCAL No.: 02-0263635
Modulation of the serological response to *meningococcal"** polysaccharides by cytokines
DE LOS ANGELES CORTES-CASTILLO Maria; THORPE R; CORBEL M J
Division of Bacteriology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Hertfordshire EN6 3QG, United Kingdom
Journal: Vaccine, 2001, 19 (30) 4194-4203
Language: English
Meningococcal A and C but not B capsular polysaccharides stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human

interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with aluminium hydroxide and outer membrane proteins. The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/ +) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals.

8/3,AB/2 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

14035645 PASCAL No.: 99-0225209
Haemophilus influenzae type b conjugate vaccine stability : catalytic depolymerization of PRP in the presence of *aluminum"** *hydroxide"**
STURGESS A W; RUSH K; CHARBONNEAU R J; LEE J I; WEST D J; SITRIN R D; HENNESSEY J P
Bioprocess and Bioanalytical Research, Merck Research Laboratories, P.O. Box 4, WP44-1130, West Point, PA 19486, United States; Vaccine Infectious Diseases, Merck Research Laboratories, 10 Sentry Parkway, Blue Bell, PA 19422, United States
Journal: Vaccine, 1999, 17 (9-10) 1169-1178
Language: English
The structural stability of the Haemophilus influenzae type b (Hib) capsular polysaccharide, polyribosylribitolphosphate (PRP) in an aluminum hydroxide adsorbed, polysaccharide -protein conjugate vaccine was monitored using modifications of an HPLC assay developed by Tsai et al. (Tsai C-M. Gu X-X. Byrd RA. Quantification of polysaccharide in Haemophilus influenzae type b conjugate and polysaccharide vaccines by high-performance anion-exchange chromatography with pulsed amperometric detection. Vaccine 1993;12:700- 706.). As applied to products containing PRP conjugated to the outer membrane protein complex (OMPC) from Neisseria meningitidis, this assay allows direct measurement of the total PRP content in very complex samples including commercial vaccine products. In addition, with the use of a high-speed centrifugation step, the assay can be used to directly quantify any PRP that is not conjugated to the OMPC carrier protein. These results provide evidence of what appears to be a catalytic reaction taking place between the phosphodiester bond of PRP and the aluminum hydroxide adjuvant that results in hydrolysis of the PRP polymer into smaller chain lengths and liberation of PRP oligomers from the conjugate particle. The reaction approaches an asymptotic limit after approximately two years at 2-8 Degree C. Clinical studies which span this time period confirm that the modest decrease in conjugated PRP content over time does not impact the overall clinical effectiveness of PRP OMPC-containing vaccines.

8/3,AB/3 (Item 1 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

12922610 References: 32
TITLE: Modulation of the serological response to *meningococcal"** polysaccharides by cytokines
AUTHOR(S): Cortes-Castillo MD; Thorpe R; Corbel MJ (REPRINT)
AUTHOR(S) E-MAIL: mcorbel@nibsc.ac.uk
CORPORATE SOURCE: Natl Inst Biol Stand & Controls, Div Bacteriol, Blanche Lane S Mimms/Potters Bar EN6 3QG/Herts/England/ (REPRINT); Natl Inst Biol Stand & Controls, Div Bacteriol, /Potters Bar EN6 3QG/Herts/England/; Natl Inst Biol Stand & Controls, Div Immunobiol, /Potters Bar EN6 3QG/Herts/England/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 2001, V19, N30 (JUL 20), P4194-4203
GENUINE ARTICLE#: 456NZ
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Meningococcal A and C but not B capsular polysaccharides stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with aluminium hydroxide and outer membrane proteins. The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/ +) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals. Crown copyright (C) 2001 Published by Elsevier Science Ltd. All rights reserved.

8/3,AB/4 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08405378 References: 44
TITLE: MF59 adjuvant enhances antibody responses of infant baboons immunized with Haemophilus influenzae type b and Neisseria *meningitidis"** group C oligosaccharide-*CRM197"** conjugate vaccine
AUTHOR(S): Granoff DM (REPRINT); McHugh YE; Raff HV; Mokatrin AS; VanNest GA
CORPORATE SOURCE: CHIRON CORP,VACCINES, 4560 HORTON ST, R-311/EMERYVILLE//CA/94608 (REPRINT); CHILDRENS HOSP,OAKLAND RES INST/OAKLAND//CA/94609
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 1997, V65, N5 (MAY), P1710-1715
GENUINE ARTICLE#: WW398

PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The ability of the adjuvant MF59 to enhance the immunogenicity of polysaccharide-protein conjugate vaccines was investigated in infant baboons, MF59 consists of stable droplets (<250 nm) of the metabolizable oil squalene and two surfactants, polyoxyethylene sorbitan monooleate and sorbitan trioleate, in an oil-in-water emulsion. In humans, MF59 is well tolerated and enhances the immunogenicity of recombinant protein subunit or particle vaccines. Its effect on the immunogenicity of polysaccharide-protein conjugate vaccines is unknown. Baboons 1 to 4 months of age were immunized intramuscularly with Neisseria meningitidis group C and Haemophilus influenzae type b (Hib) oligosaccharide-CRM197 conjugate vaccines. The lyophilized vaccines were reconstituted with phosphate-buffered saline (PBS), Al(OH)(3) (alum), or MF59. Groups of five animals each were given three injections of the respective formulations, with one injection every 4 reeks. Four weeks after each immunization, the MF59 group had up to 7-fold-higher geometric mean anticapsular-antibody titers than the alum group and 5- to 10-fold-higher N. meningitidis group C bactericidal-antibody titers. Twenty one weeks after the third immunization, the MF59 group still showed 5- to 10-fold-higher anticapsular-antibody titers, The antibody responses of the animals given the vaccines reconstituted with PBS were low at all times measured, Both the MF59 and alum groups, but not the PBS group, showed booster antibody responses to unconjugated Hib and N. meningitidis group C polysaccharides, results consistent with induction of memory B cells. Thus, MF59 may be useful for accelerating and augmenting immunity to polysaccharide-protein conjugate vaccines in infants.

8/3,AB/5 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06820836 References: 34
TITLE: ANTIBODY RESPONSE AFTER IMMUNIZATION OF BRAZILIAN CHILDREN WITH SEROGROUP C *MENINGOCOCCAL"** POLYSACCHARIDE NONCOVALENTLY COMPLEXED WITH *OUTER"** *MEMBRANE"** *PROTEINS"**
AUTHOR(S): MILAGRES LG; LEMOS APS; MELES CEA; SILVA EL; FERREIRA LHML; SOUZA JAM; CARLONE GM
CORPORATE SOURCE: INST ADOLFO LUTZ REGISTRO,SECAO BACTERIOL,AV DRARNALDO 351,CERQUEIRA CESAR/BR-01246902 SAO PAULO//BRAZIL/ (Reprint); LAB CENT SAUDE PUBL/BR-68906970 MACAPA/AMAPA/BRAZIL/; CTR SAUDE 1/BR-13870000 SAO JOAO BOA/SP/BRAZIL/; CTR REG SAUDE,ERSA 54/BR-13870000 SAO JOAO BOA/SP/BRAZIL/; CTR DIS CONTROL & PREVENT,CHILDHOOD & RESP DIS BRANCH/ATLANTA//GA/30333
PUBLICATION: BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH, 1995, V 28, N9 (SEP), P981-989
GENUINE ARTICLE#: RZ771
ISSN: 0100-879X
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: We have studied the antibody response of Brazilian vaccinees to C meningococcal polysaccharide (C-PS) after one or two doses of a vaccine composed of C-PS, outer membrane proteins of B meningococci and aluminum hydroxide. Total IgG, IgG1 and IgG2 as well as bactericidal activity

mediated by complement were measured in serum samples from children 3 to 83 months of age (postvaccination IgG, IgG1 and IgG2 levels of 2.4 to 13.4 mu g/ml; less than 18 to 67.8 U/ml and less than 18 to 106.8 U/ml, respectively) and from individuals 10 to 14 years of age (post-vaccination IgG, IgG1 and IgG2 levels of 14.6 mu g/ml, 23.7 U/ml and 112.0 U/ml, respectively). The antibody response, measured as IgG levels, was age-dependent. Although high antibody levels were demonstrable by enzyme-linked immunosorbent assay (ELISA), bactericidal activity was not demonstrable (less than 1:4 in serum from children aged less than 24 months. A significant bactericidal activity was detected in serum of children older than 49 months of age and in individuals 10 to 14 years of age. A predominance of IgG2 was observed in post-vaccination serum samples from children belonging to those two age groups. The antibody concentration sufficient to confer protection as well as the possible causes of the poor correlation observed between ELISA and bactericidal activity results are discussed.

8/3,AB/6 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05537533 References: 46
TITLE: IMMUNE RESPONSES OF YOUNG MICE TO PNEUMOCOCCAL TYPE 9V POLYSACCHARIDE-TETANUS *TOXOID"** CONJUGATE
AUTHOR(S): LU CH; LEE CJ; KIND P (Reprint)
CORPORATE SOURCE: GEORGE WASHINGTON UNIV,SCH MED & HLTH SCI,DEPT MICROBIOL & IMMUNOL/WASHINGTON//DC/20037 (Reprint); GEORGE WASHINGTON UNIV,SCH MED & HLTH SCI,DEPT MICROBIOL & IMMUNOL/WASHINGTON//DC/20037; CTR BIOL EVALUAT & RES/BETHESDA//MD/20892
PUBLICATION: INFECTION AND IMMUNITY, 1994, V62, N7 (JUL), P2754-2760
GENUINE ARTICLE#: NU014
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Pneumococcal type 9V polysaccharide (PS), contained in the current pneumococcal vaccine, induces only a weak antibody response in young children and therefore is not an effective vaccine for young children. To increase its immunogenicity, a conjugate of PS to a protein carrier, tetanus toroid (TT), was prepared. To quantify the immune response, mouse anti-9V PS immunoglobulin G (IgG) and IgM reference standards were established. Young mice immunized at 2 weeks of age produced IgM antibody in response to 9V PS alone or 9V PS conjugated to TT. However, only the 9V PS-TT conjugate induced an IgG antibody response and an anamnestic effect. Thus, a covalent linkage between TT and 9V PS was required for isotype switching from IgM to IgG. 9V PS-TT adsorbed with aluminum hydroxide adjuvant resulted in a fivefold or greater increase in the IgG antibody level. We also studied the effect of maternal immunization on the immune response of young mice to 9V PS-TT. Maternal immunization before mating or before mating and during gestation primed 2-week-old progeny given two injections of 9V PS-TT to produce more IgM antibody than progeny from unimmunized mothers. The IgG antibody level of neonates at birth was similar to that observed in the mothers and was probably passive antibody. These results indicate that maternal immunization with an optimum dose of a PS-protein conjugate before and/or during pregnancy, followed by immunization of the offspring with the conjugate, could provide young children with an enhanced IgM antibody response to pneumococcal PSs.

8/3,AB/7 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03275704 References: 67
TITLE: PREPARATION, CHARACTERIZATION, AND IMMUNOGENICITY OF CONJUGATES COMPOSED OF THE O-SPECIFIC POLYSACCHARIDE OF SHIGELLA-DYSENTERIAE TYPE-1 (SHIGA BACILLUS) BOUND TO TETANUS *TOXOID"**
AUTHOR(S): CHU CY; LIU BK; WATSON D; SZU SS; BRYLA D; SHILOACH J; SCHNEERSON R; ROBBINS JB (Reprint)
CORPORATE SOURCE: NICHHD,DEV & MOLEC IMMUN LAB/BETHESDA//MD/20892 (Reprint); NICHHD,DEV & MOLEC IMMUN LAB/BETHESDA//MD/20892; NICHHD,BIOMETRY & MATH STAT BRANCH/BETHESDA//MD/20892; NIDDKD,CELLULAR & MOLEC BIOL LAB,BIOTECHNOL UNIT/BETHESDA//MD/20892
PUBLICATION: INFECTION AND IMMUNITY, 1991, V59, N12 (DEC), P4450-4458
GENUINE ARTICLE#: GR214
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The background for developing conjugate vaccines for shigellosis composed of the O-specific polysaccharide (O-SP) bound to a protein is described elsewhere (C. Y. Chu, R. Schneerson, and J. B. Robbins, submitted for publication). Briefly, there is direct evidence for type (lipopolysaccharide [LPS])-specific protection after infection with the wild type or with attenuated strains of shigellae. Prospective studies of Israeli armed forces recruits show a correlation between preexisting serum immunoglobulin G (IgG) LPS antibodies and resistance to shigellosis (D. Cohen, M. S. Green, C. Block, R. Slephon, and I. Ofek, J. Clin. Microbiol. 29:386-389, 1991). In order to elicit IgG LPS-specific antibodies to Shigella dysenteriae type 1, the O-SP of this pathogen was purified and bound to tetanus toxoid (TT) by three schemes. The most immunogenic used a modification of a published method (C. Y. Chu, R. Schneerson, J. B. Robbins, and S. C. Rastogi, Infect. Immun. 40:245-256, 1983). The resultant O-SP-TT conjugates were stable and elicited high levels of IgG O-SP antibodies and booster responses in young mice when injected subcutaneously in saline at 1/10 the proposed human dose. Adsorption onto alum or concurrent administration with monophosphoryl lipid A enhanced both the IgG and IgM antibody responses to the O-SP of the conjugate; both the nonadsorbed and adsorbed conjugates elicited higher rises of IgG than of IgM antibodies. Clinical evaluations of S. dysenteriae type 1 O-SP-TT conjugates are planned.

8/3,AB/8 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03123010 References: 34
TITLE: HUMAN IGA1 BLOCKADE OF IGG-INITIATED LYSIS OF NEISSERIA-*MENINGITIDIS"** IS A FUNCTION OF ANTIGEN-BINDING FRAGMENT BINDING TO THE *POLYSACCHARIDE"** *CAPSULE"**
AUTHOR(S): JARVIS GA; GRIFFISS JM
CORPORATE SOURCE: VET ADM MED CTR,4150 CLEMENT ST/SAN FRANCISCO//CA/94121 (Reprint); UNIV CALIF LOS ANGELES,CTR IMMUNOCHEM,DEPT LAB MED/LOS ANGELES//CA/90024; UNIV CALIF LOS ANGELES,DEPT MED/LOS ANGELES//CA/90024
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1991, V147, N6 (SEP 15), P1962-1967
GENUINE ARTICLE#: GG108
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: We have recently shown that human IgA1 can initiate lysis of group C Neisseria meningitidis via the classical C pathway when bound to specific outer membrane proteins, but that IgA1 can also function as a blocking antibody when bound to the polysaccharide capsule of meningococci. In this report, we further characterized IgA1 blockade by examining the effect of IgA1 on IgG-initiated immune lysis of group C meningococci. We purified IgG and monomeric IgA1 from either convalescent group C meningococcal case sera or tetravalent (A, C, Y, W135) polysaccharide vaccinate sera. In the absence of IgA1, IgG initiated complete lysis (> 99%) of strains 118V (C:P3,4:L2,4) 126E (C:P3:L1,8), and 35E (C:P5:L2). Addition of IgA1 to the bactericidal reaction mixture completely blocked the lytic function of IgG. Removal of the Fc portion of IgA1 with either pepsin or IgA1 protease did not affect blockade. Both the F(ab')2 and Fab derivatives of IgA1 blocked lysis quantitatively as well as intact IgA1. The Fc fragment produced by IgA1 protease cleavage neither increased nor decreased Fab-mediated blockade. IgA1 and its Fab and F(ab')2 fragments blocked IgG-initiated lysis via either the classical pathway in factor B-depleted and in properdin-deficient serum, the alternative pathway in MgEGTA-chelated serum, or both pathways combined. Absorption of the IgA1 and IgG with alum-bound group C polysaccharide completely removed blocking and lytic activity, respectively, indicating that both the blocking IgA1 and the lytic IgG were specific for the group C capsule. Blocking by IgA1 was a linear function of the polysaccharide Ag-binding capacity (ABC) ratio of blocking IgA1 to lytic IgG. Complete blockade was observed at an ABC ratio of 5.5. At ABC ratios of 3.3 and 4.4, IgA1 affected significant blockade whether added previous to, concurrent with, or subsequent to sensitization of the organisms with IgG. With the use of a C polysaccharide ELISA, we found that the binding of IgA1 to the group C capsule in the presence of IgG exhibited positive cooperativity and therefore that blockade was independent of the ability of IgA1 to directly compete with IgG for binding to epitopes within the group C capsule. We conclude that IgA1, when bound to the group C polysaccharide capsule, can block IgG-initiated lysis of group C meningococci through either the classical or the alternative pathway before or after the organism is exposed to IgG, and that blockade is an Fc-independent event.

8/3,AB/9 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02498176 References: 31
TITLE: IMMUNOGENICITY IN ADULT MALES OF A NEISSERIA-*MENINGITIDIS"** GROUP-B VACCINE COMPOSED OF POLYSACCHARIDE COMPLEXED WITH *OUTER"** *MEMBRANE"** *PROTEINS"**
AUTHOR(S): LIFELY MR; ROBERTS SC; SHEPHERD WM; ESDAILE J; WANG Z; CLEVERLY A; AULAQI AA; MORENO C
CORPORATE SOURCE: WELLCOME BIOTECH,DEPT EXPTL IMMUNOBIOL,LANGLEY COURT/BECKENHAM BR3 3BS/KENT/ENGLAND/ (Reprint); WELLCOME FDN LTD,DEPT CLIN RES/BECKENHAM BR3 3BS/KENT/ENGLAND/; WELLCOME FDN LTD,DEPT SCI COMP STAT/BECKENHAM BR3 3BS/KENT/ENGLAND/; WELLCOME INT TRADING LTD,MED ADVISORY SERV/BERKHAMSTED HP4 2DY/HERTS/ENGLAND/; HAMMERSMITH HOSP,MRC,TB & RELATED INFECT UNIT/LONDON W12 0HS//ENGLAND/
PUBLICATION: VACCINE, 1991, V9, N1 (JAN), P60-66
GENUINE ARTICLE#: EQ328
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Twenty five adult male volunteers were given a vaccine composed of the capsular B polysaccharide non-covalently complexed to serotype 6 outer membrane proteins (OMP) of Neisseria meningitidis. Subjects were divided into three dose groups receiving 50, 100 or 150-mu-g vaccine in aluminium hydroxide in each of three injections spaced 4 weeks apart. Systemic signs/symptoms considered clinically significant were recorded on 6% (4/70) of occasions and were succeeded by withdrawal of two volunteers from the study. Local injection site reactions, mostly mild to moderate, were reported after all vaccinations with one such reaction leading to a third volunteer withdrawing from the study. Geometric mean anti-B responses before immunization and 1 week after the third immunization (9 weeks) were 3.60 and 7.12-mu-g ml-1 in the 50-mu-g group ($p < 0.05$), 2.05 and 12.19-mu-g ml-1 in the 100-mu-g group ($p < 0.001$), and 3.68 and 14.20-mu-g ml-1 in the 150-mu-g group ($p < 0.001$). The anti-B response was predominantly of the IgM isotype and persistence above prevaccination levels was evident for at least 12 months. Anti-type 6 OMP responses were also evidenced with geometric mean multiplicative increases over prevaccination levels at 9 weeks and 6 months of 7.8 and 4.2 for the 50-mu-g group, 11.6 and 5.6 for the 100-mu-g group and 6.8 and 3.4 for the 150-mu-g group. The bulk of this response was of the IgG isotype. Passive protection of mice was achieved with both pre- and post-vaccination (9 weeks; 100 and 150-mu-g groups) pools of sera. Protection was abolished by prior adsorption of sera with B polysaccharide.

8/3,AB/10 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00935584
NEISSERIA *MENINGITIDIS"** SEROGROUP B GLYCOCONJUGATES AND METHODS OF USING THE SAME
NEISSERIA *MENINGITIDIS"** SEROGRUPPE B GLYKOKONJUGATE UND VERFAHREN ZU DEREN VERWENDUNG
GLYCOCONJUGUES DU GROUPE SEROLOGIQUE B DE NEISSERIA *MENINGITIDIS"** ET PROCEDES POUR LEUR UTILISATION
PATENT ASSIGNEE:
CHIRON CORPORATION, (572530), 4560 Horton Street, Emeryville, California 94608, (US), (Proprietor designated states: all)
INVENTOR:
SEID, Robert, C., 737 Peru Street, San Francisco, CA 94112, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), CARPMAELS AND RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 939647 A1 990908 (Basic)
EP 939647 B1 011114
WO 9808543 980305
APPLICATION (CC, No, Date): EP 97936364 970804; WO 97US13609 970804
PRIORITY (CC, No, Date): US 24454 P 960827
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/385
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200146	1132

CLAIMS B	(German)	200146	1071
CLAIMS B	(French)	200146	1338
SPEC B	(English)	200146	9020

Total word count - document A 0
Total word count - document B 12561
Total word count - documents A + B 12561

8/3,AB/11 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00832984
A VACCINE COMPOSITION COMPRISING A POLYSACCHARIDE CONJUGATE ANTIGEN ADSORBED ONTO *ALUMINIUM"** *PHOSPHATE"**
EINE IMPFSTOFFZUSAMMENSETZUNG,BESTEHEND AUS EINEM POLYSACCHARID ANTIGEN-KONJUGATADSORBIERT AN ALUMINIUMPHOSPHAT
COMPOSITION DE VACCIN COMPORTANT UN ANTIGENE POLYOSIDIQUE CONJUGUE ADSORBE SUR DU PHOSPHATE D'ALUMINIUM
PATENT ASSIGNEE:
SMITHKLINE BEECHAM BIOLOGICALS S.A., (1311860), 89 rue de l'Institut, 1330 Rixensart, (BE), (Proprietor designated states: all)
INVENTOR:
PEETERMANS, Julien, Rue de l'Institut 89, B-1330 Rixensart, (BE)
HAUSER, Pierre, Rue de l'Institut 89, B-1330 Rixensart, (BE)
LEGAL REPRESENTATIVE:
Dalton, Marcus Jonathan William (60102), SmithKline Beecham plc Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP, (GB)
PATENT (CC, No, Kind, Date): EP 833662 A1 980408 (Basic)
EP 833662 B1 010321
WO 9700697 970109
APPLICATION (CC, No, Date): EP 96922871 960619; WO 96EP2690 960619
PRIORITY (CC, No, Date): GB 9512827 950623; GB 9513443 950701; GB 9525657 951215; GB 9606032 960322
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: SI
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1082965 (EP 203874)
INTERNATIONAL PATENT CLASS: A61K-039/39; A61K-039/145
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200112	432
CLAIMS B	(German)	200112	399
CLAIMS B	(French)	200112	504
SPEC B	(English)	200112	2089

Total word count - document A 0
Total word count - document B 3424
Total word count - documents A + B 3424

8/3,AB/12 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00804486
Neisseria *meningitidis"** *capsular"** *polysaccharide"** conjugates
Konjugate von Neisseria *Meningitidis"** Kapselpolysacchariden
Composes conjugues a partir de *polysaccharides"** *capsulaires"** de Neisseria *meningitidis"**
PATENT ASSIGNEE:
CONNAUGHT LABORATORIES LIMITED, (267451), 1755 Steeles Avenue West, Willowdale Ontario M2R 3T4, (CA), (applicant designated states: BE;DE;FR;GB;IT)
INVENTOR:
Kandil, Ali, 245 Park Home Avenue, Willowdale, Ontario M2R 1A1, (CA)
Klein, Michel H., 16 Munro Boulevard, Willowdale, Ontario M2P 1B9, (CA)
Chong, Pele, 32 Estoril Street, Richmond Hill, Ontario L4C 0E6, (CA)
LEGAL REPRESENTATIVE:
Smart, Peter John (43071), W.H. BECK, GREENER & CO 7 Stone Buildings Lincoln's Inn, London WC2A 3SZ, (GB)
PATENT (CC, No, Kind, Date): EP 747063 A2 961211 (Basic)
EP 747063 A3 990324
APPLICATION (CC, No, Date): EP 96304311 960607;
PRIORITY (CC, No, Date): US 474392 950607
DESIGNATED STATES: BE; DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-039/095;

ABSTRACT EP 747063 A2
Capsular polysaccharides containing multiple sialic acid residues, particularly the Group B polysaccharide of Neisseria meningitidis, are modified by chemical reaction to randomly introduce pendant reactive residues of heterobifunctional linker molecules to the polysaccharide backbone. The capsular polysaccharide is deacetylated and the heterobifunctional linker molecule is reacted with the deacetylated material and any residual amino groups are blocked by reaction with alkyl acid anhydride. The introduction of the linker molecules to the polysaccharide chain between the termini enables the polysaccharide to be linked to a carrier molecule, such as a protein, to enhance the immunogenicity of the polysaccharide. The conjugate molecule may be formulated as an immunogenic composition for raising antibodies in a host to the polysaccharide.
ABSTRACT WORD COUNT: 138

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	718
SPEC A	(English)	EPAB96	6289
Total word count - document A			7007
Total word count - document B			0
Total word count - documents A + B			7007

8/3,AB/13 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00646348
Preparation and uses of LOS-depleted *outer"** *membrane"** *proteins"** of gram-negative cocci
Herstellung und Verwendungen von LOS-verminderten Aussenmembran-Proteinen

von Gram-negativen Kokken
Preparation et utilisations de proteines de membranes externes depouvues de LOS a partir de coques gram-negatifs
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212592), One Cyanamid Plaza, Wayne New Jersey 07470, (US), (Proprietor designated states: all)
INVENTOR:
Zlotnick, Gary W., 21 Woodlyn Way, Penfield, New York 14526, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt, Tal 29, 80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 624376 A1 941117 (Basic)
EP 624376 B1 000315
APPLICATION (CC, No, Date): EP 94106827 940502;
PRIORITY (CC, No, Date): US 61581 930513
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
EXTENDED DESIGNATED STATES: SI
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/40

ABSTRACT EP 624376 A1
Described herein is a method for removing toxic lipooligosaccharide (LOS) from outer membranes of Gram-negative cocci, such as Neisseria meningitidis. LOS-depleted outer membranes and LOS-depleted soluble outer membrane proteins can be prepared, which are able to elicit bactericidal antibodies against homologous strains of bacteria. Vaccines and other uses of the preparations are further described.
ABSTRACT WORD COUNT: 56
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200011	865
CLAIMS B	(German)	200011	798
CLAIMS B	(French)	200011	1006
SPEC B	(English)	200011	5445
Total word count - document A			0
Total word count - document B			8114
Total word count - documents A + B			8114

8/3,AB/14 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00619892
VACCINES AGAINST GROUP C NEISSERIA *MENINGITIDIS"**
IMPFSTOFFE GEGEN NEISSERIA *MENINGITIDIS"** GRUPPE C
VACCINS CONTRE LA NEISSERIA *MENINGITIDIS"** DU GROUPE C
PATENT ASSIGNEE:
Baxter Healthcare S.A., (3374410), Hertistrasse 2, 8306 Wallisellen, (CH), (Proprietor designated states: all)
INVENTOR:
MICHON, Francis, 4401 Rosedale Avenue, Bethesda, MD 20814, (US)
JENNINGS, Harold, 2049 Woodglen Crescent, Gloucester, Ontario, Canada K1J6 G6, (CA)

TAI, Joseph Y., 1370 Cinnamon Drive-Fort Washington, Pennsylvania 19034, (US)
HRONOWSKI, Lucjan J.J., 9160F Hitching Post Lane Laurel, Maryland 20723, (US)
MATES, Sharon, 5610 Wisconsin Avenue, Apt. 1504, Chevy Chase, Maryland 20815, (US)
LEGAL REPRESENTATIVE:
Laufhutte, Dieter, Dr.-Ing. et al (61841), Lorenz-Seidler-Gossel Widenmayerstrasse 23, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 658118 A1 950621 (Basic)
EP 658118 A1 950913
EP 658118 B1 020123
WO 9405325 940317
APPLICATION (CC, No, Date): EP 93921251 930830; WO 93US8155 930830
PRIORITY (CC, No, Date): US 938367 920831; US 64501 930519
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/385; A61K-039/40; C07H-001/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200204	334
CLAIMS B	(German)	200204	319
CLAIMS B	(French)	200204	392
SPEC B	(English)	200204	5372
Total word count - document A			0
Total word count - document B			6417
Total word count - documents A + B			6417

8/3,AB/15 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00536407
*Pneumococcal"** *polysaccharide"** conjugate vaccine
Imfpstoff, enthaltend ein Pneumokokkenpolysaccharid-Konjugat
Vaccin a base de conjugue de polysaccharide de pneumocoque
PATENT ASSIGNEE:
Merck & Co., Inc., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;PT;SE)
INVENTOR:
Kniskern, Peter J., 841 Patterson Drive, Lansdale, PA 19446, (US)
Ip, Charlotte C., 1665 Chadwyck Place, Blue Bell, PA 19422, (US)
Hagopian, Arpi, 771 Hartley Drive, Lansdale, PA 19446, (US)
Hennessey Jr., John P., 114 Fox Hollow Road, Dublin, PA 18917, (US)
Miller, William J., 232 Old Church Road, North Wales, PA 19454, (US)
Kubek, Dennis J., 76 Carolina Avenue, Salem, West Virginia 26426, (US)
Burke, Pamela D., 862 Yorktown Street, Landsdale, PA 19446, (US)
Marburg, Stephen, 50 Concord Avenue, Metuchen, NJ 08840, (US)
Tolman, Richard L., 29 Upper Warren Way, Warren, NJ 07059, (US)
LEGAL REPRESENTATIVE:
Thompson, John Dr. et al (62771), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow, Essex CM20 2QR, (GB)

PATENT (CC, No, Kind, Date): EP 497525 A2 920805 (Basic)
EP 497525 A3 930310
EP 497525 B1 980819
APPLICATION (CC, No, Date): EP 92300655 920127;
PRIORITY (CC, No, Date): US 646570 910128; US 807942 911219
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/09; A61K-039/095; A61K-039/295; A61K-039/02; A61K-047/48;

ABSTRACT EP 497525 A2
A novel conjugate vaccine comprising partially hydrolyzed, highly purified, capsular polysaccharide (Ps) from Streptococcus pneumoniae bacteria (pneumococci, Pn) linked to an immunogenic carrier protein, is produced by a new process. The conjugate is useful in the prevention of pneumococcal infections. Vaccines comprising a mixture of from one to ten different pneumococcal polysaccharide-immunogenic protein (Pn-Ps-PRO) conjugates induce broadly protective recipient immune responses against the cognate pathogens from which the polysaccharide components are derived. Young children and infants younger than 2 years old, normally unable to mount a protective immune response to the Pn-Ps alone, exhibit protective immune responses upon vaccination with these Pn-Ps-PRO conjugates.
ABSTRACT WORD COUNT: 105

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9834	1182
CLAIMS B	(German)	9834	1225
CLAIMS B	(French)	9834	1373
SPEC B	(English)	9834	25880
Total word count - document A			0
Total word count - document B			29660
Total word count - documents A + B			29660

8/3,AB/16 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00498481
IMPROVED *MENINGOCOCCAL"** *POLYSACCHARIDE"** CONJUGATE VACCINE.
VERBESSERTES MENINGOKOKKALE POLYSACCHARIDKONJUGATVAKZIN.
VACCIN CONJUGUE AMELIORE A BASE DE POLYSACCHARIDE DE MENINGOCOQUE.
PATENT ASSIGNEE:
NATIONAL RESEARCH COUNCIL OF CANADA, (487624), Montreal Road, Ottawa Ontario K1A OR6, (CA), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
JENNINGS, Harold, J., 2049 Woodglen Crescent, Gloucester, ON, K1J 6G6, (CA)
MICHON, Francis, 128 Keefer Street, Ottawa, ON, K1M 1T5, (CA)
LEGAL REPRESENTATIVE:
Laufhutte, Dieter, Dr.-Ing. et al (61841), Lorenz-Seidler-Gossel Widenmayerstrasse 23, D-80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 504202 A1 920923 (Basic)
EP 504202 B1 950503

WO 9108772 910627
APPLICATION (CC, No, Date): EP 91900142 901213; WO 90CA437 901213
PRIORITY (CC, No, Date): US 448195 891214
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/108; A61K-039/385;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	535
CLAIMS B	(German)	EPAB95	471
CLAIMS B	(French)	EPAB95	607
SPEC B	(English)	EPAB95	4342
Total word count - document A			0
Total word count - document B			5955
Total word count - documents A + B			5955

8/3,AB/17 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00485895
The class II protein of the outer membrane of neisseria *meningitidis"**.
Klasse-II-Protein der ausseren Membran von Neisseria *meningitidis"** und dasselbe enthaltende Impfstoffe.
Classe II de la membrane exterieure de Neisseria *meningitidis"** et raccins la contenant.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Oliff, Allen I., 1412 Florence Drive, Gwynedd Valley, PA 19437, (US)
Liu, Margaret A., 4 Cushman Road, Rosemont, PA 19190, (US)
Friedman, Arther, 121 Froghollow Road, Churchville, PA 18966, (US)
Tai, Joseph Y., 1370 Cinnamon Drive, Fort Washington, PA 19034, (US)
Donnelly, John J., 1505 Briarwood Road, Havertown, PA 19083, (US)
Jones, Deborah D., 1126 Canterbury Drive, Lansdale, PA 19446, (US)
Montgomery, Donna L., 9 Hickory Lane, Chalfont, PA 18914, (US)
Lowe, Robert S., 232 Maple Avenue, Harleysville, PA 19438, (US)
LEGAL REPRESENTATIVE:
Barrett-Major, Julie Diane et al (50911), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 467714 A1 920122 (Basic)
APPLICATION (CC, No, Date): EP 91306618 910719;
PRIORITY (CC, No, Date): US 555329 900719; US 555204 900719; US 555978 900719; US 639457 910110; US 715274 910619
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-013/00; C07K-003/28; C12N-015/09; A61K-039/39; A61K-039/095;

ABSTRACT EP 467714 A1
The Class II major immuno-enhancing protein (MIEP) of Neisseria meningitidis, purified directly from the outer membrane of Neisseria meningitidis, or obtained through recombinant cloning and expression of

DNA encoding the MIEP of Neisseria meningitidis, has immunologic carrier as well as immunologic enhancement and mitogenic properties.
ABSTRACT WORD COUNT: 47

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1309
SPEC A	(English)	EPABF1	25077
Total word count - document A			26386
Total word count - document B			0
Total word count - documents A + B			26386

8/3,AB/18 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00478178
Nucleotide sequence coding for an *outer"** *membrane"** *protein"** from Neisseria *meningitidis"** and use of said protein in vaccine preparations
Nukleotidsequenz, die fur ein Aussenmembran-Protein von Neisseria *meningitidis"** kodiert und Verwendung dieses Proteins zur Herstellung von Impfstoffen
Sequence nucleotidique codant pour une proteine de la membrane externe de Neisseria *meningitidis"** , et utilisation de cette proteine dans la preparation de vaccin
PATENT ASSIGNEE:
CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA, (1256830), 31 Street, '/156 & 190, Cubanacan Playa, Havana, (CU), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Rodriguez, Ricardo Silva, Calle 15 No. 4209, entre 42 y 44, Playa, La Habana, (CU)
Houssein Sosa, Manuel Selman, Paseo No. 126, entre 5ta y Calzada, Vedado, La Habana, (CU)
Nieto, Gerardo Guillen, Linea No.6, Apto 4, entre N y O, Vedado, La Habana, (CU)
Herrera Martinez, Luis S. Centro Ingenieria, Genetica y Biotecnoligia 31 Str., '/156 & 190, Cubanacan. Playa Havana, (CU)
Fernandez Maso, Julio RaUl, Calle 26 No.873 1-2,Apto 3, entre Conill y45,Nuevo, La Habana, (CU)
Novoa Perez, Lidia Ines, Calle 184 No.3112, entre 31 y 33, Apto 49, Playa , La Habana, (CU)
Grillo, Juan Morales, Compostela No.653, Apto 1, entre Luz y Acosta, Habana Vieja, La Habana, (CU)
Morera Cordova, Vivian, Calle 184 No.3112, entre 31 y 33, Apto 39, Playa, La Habana, (CU)
Gonzalez Blanco, Sonia, Calle 184 No.3112, entre 31 y 33, Apto 42, Playa, La Habana, (CU)
Santos, Beatriz Tamargo, Calle 202 No.29302, entre 293y295, Reparto Calixto, Sanchez, Boyeros, La Habana, (CU)
del Valle Rosales, JesUs Augusto, D'Strampes N.351, entre San Mariano y Vista Alegre, La Vibora, La Habana, (CU)
Menendez, Evelin Caballero, Calle 7 No.214, entre 2 y 4, Cayo de la Rosa, Bauta, La Habana, (CU)
Alvarez Acosta, Anabel, Calle 184 No.3112, entre 31 y 33, Apto 1, Playa,

La Habana, (CU)
Couzeau Rodriguez, Edelgis, Calle 184 No.3112, entre 31 y 33, Apto 20, Playa, La Habana, (CU)
Cruz Leon, Silian, Ave 47 No.11812, entre 118 y 120, Marianao, La Habana, (CU)
Musacchio Lasa, Alexis, Calle 128 No.7117, entre 71 y 73, Mariel, La Habana, (CU)
LEGAL REPRESENTATIVE:
Smulders, Theodorus A.H.J., Ir. et al (21191), Vereenigde Octrooibureaux Nieuwe Parklaan 97, 2587 BN 's-Gravenhage, (NL)
PATENT (CC, No, Kind, Date): EP 474313 A2 920311 (Basic)
EP 474313 A3 930224
EP 474313 B1 970423
APPLICATION (CC, No, Date): EP 91202291 910906;
PRIORITY (CC, No, Date): CU 14590 900907
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; A61K-039/095; C12P-021/08; C12N-015/62; C12N-015/53; C12N-015/54; C12N-001/21; C12N-001/21; C12R-001/19

ABSTRACT EP 474313 A2
The present invention is concerned with a method for the isolation of a nucleotide sequence which codes for a protein having a molecular weight of about 64 000 daltons, which is located on the outer membrane of N. meningitidis, as well as with the recombinant DNA obtained therefrom, which is used for the transformation of a host microorganism. The technical object pursued with the invention is the identification of a nucleotide sequence coding for a highly conserved and common protein for the majority of pathogenic Neisseria strains, the production of this protein with a high level of purity and in commercially useful amounts using the recombinant way, so that it can be used in diagnostic methods and vaccine preparations with a broad immunoprotection spectrum. (see image in original document)
ABSTRACT WORD COUNT: 131

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	765
CLAIMS B	(English)	EPAB97	305
CLAIMS B	(German)	EPAB97	313
CLAIMS B	(French)	EPAB97	323
SPEC A	(English)	EPABF1	6148
SPEC B	(English)	EPAB97	6260
Total word count - document A			6913
Total word count - document B			7201
Total word count - documents A + B			14114

8/3,AB/19 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00443912
*MENINGOCOCCAL"** CLASS 1 *OUTER"**-*MEMBRANE"** *PROTEIN"** VACCINE
*MENINGOCOCCALES"** KLASSE I-AUSSENMEMBRANPROTEIN-VAKZIN
VACCIN MENINGOCOQUE DE LA PROTEINE DE LA MEMBRANE EXTERNE DE LA CLASSE 1
PATENT ASSIGNEE:

AMERICAN CYANAMID COMPANY, (212595), One Portland Square, Portland, Maine 04101, (US), (Proprietor designated states: all)
De Staat der Nederlanden, represented by the Deputy Director-General of the RIVM of Bilthoven, (935230), Antonie van Leeuwenhoeklaan 9, NL-3720 BA Bilthoven, (NL), (Proprietor designated states: all)
INVENTOR:
SEID, Robert, C., Jr., 590 25th Avenue, San Francisco, CA 94121, (US)
PARADISO, Peter, R., 6 Guilford Way, Pittsford, NY 14534, (US)
POOLMAN, Jan, T., Leeteinde 8, NL-1151 AK Broek in Waterland, (NL)
HOOGERHOUT, Peter, Idenburgstraat 13, NL-2805 SZ Gouda, (NL)
WIERTZ, Emmanuel, J., H., J., Mauritsstraat 106, NL-3583 HW Utrecht, (NL)
VAN DER LEY, Peter, Adriaan van Ostadelaan 124, NL-3583 AM Utrecht, (NL)
HECKELS, John, Edward 6 Arun Way West Wellow, Romsey, Hampshire SO51 6GT, (GB)
CLARKE, Ian, Nicholas 15 Fernyhurst Avenue, Rownhams Southampton, Hampshire SO1 8DR, (GB)
LEGAL REPRESENTATIVE:
Roques, Sarah Elizabeth et al (79543), J.A. Kemp & Co. 14 South Square Gray's Inn, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 449958 A1 911009 (Basic)
EP 449958 B1 950322
EP 449958 B2 021113
WO 90006696 900628
APPLICATION (CC, No, Date): EP 90901397 891219; WO 89US5678 891219
PRIORITY (CC, No, Date): NL 883111 881219; NL 8936 890106; NL 891612 890626
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; C07K-014/22; C07K-007/04; A61K-039/39; A61K-039/385; C12N-015/31; C12N-015/62; C12N-15:31; C12R-1:36
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200246	2221
CLAIMS B	(German)	200246	2207
CLAIMS B	(French)	200246	2873
SPEC B	(English)	200246	14431
Total word count - document A			0
Total word count - document B			21732
Total word count - documents A + B			21732

8/3,AB/20 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00339312
Haemophilus influenzae type B polysaccharide-*outer"** *membrane"** *protein"** conjugate vaccine.
Haemophilus influenzae Typ B Polysaccharid-Aussermembranprotein-Konjugat als Impfstoff.
Vaccin a base d'un conjugat de proteine de membrane externe et de polysaccharide de type B d'haemophilus influenzae.
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212594), One Cyanamid Plaza, Wayne, NJ 07470-8426, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;NL;SE)

INVENTOR:
Kuo, Joseph S.-C., 67 Constitution Drive, Tappan, NY 10983, (US)
Bristol, James Edwin, 58 North Serven Street, Pearl River, NY 10965, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Dr. (12711), Tal 29, D-80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 338265 A2 891025 (Basic)
EP 338265 A3 891213
EP 338265 B1 940504
APPLICATION (CC, No, Date): EP 89104996 890321;
PRIORITY (CC, No, Date): US 183206 880419
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/102;

ABSTRACT EP 338265 A2
Immunogenic conjugates of a 38,000 daltons or 40,000 daltons outer membrane protein of H. Influenzae type b and oxidized polyribosyl-ribitol-phosphate polysaccharide fragments of H. influenzae type b are disclosed. Vaccines containing the conjugates are disclosed as useful in immunizing against H. Influenzae type b caused disease. Methods for isolating and purifying the 38,000 daltons and 40,000 daltons outer membrane proteins and for preparing the oxidized polyribosyl-ribitol-phosphate polysaccharide fragments are also disclosed.
ABSTRACT WORD COUNT: 75

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPBBF1	715
CLAIMS B	(English)	EPBBF1	975
CLAIMS B	(German)	EPBBF1	893
CLAIMS B	(French)	EPBBF1	1183
SPEC A	(English)	EPBBF1	6020
SPEC B	(English)	EPBBF1	5924
Total word count - document A			6735
Total word count - document B			8975
Total word count - documents A + B			15710

8/3,AB/21 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00187286
Covalently-modified neutral *bacterial"** *polysaccharides"** , stable covalent conjugates of such polysaccharides and immunogenic proteins, and methods of preparing suc
Kovalentlich modifizierte neutrale bakterielle Polysaccharide, stabile kovalente Konjugate zwischen diesen Polysacchariden und immunogenischen Proteinen und Ver
Polysaccharides bacteriens neutres modifies de maniere covalente, conjuges stables covalents entre ces polysaccharides et des proteines immunogeniques et method
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:

Marburg, Stephen, 50 Concord Avenue, Metuchen New Jersey 08840, (US)
Tolman, Richard L., 29 Upper Warren Way, Warren New Jersey 07060, (US)
Jorn, Deborah A., 27 Ticonderoga Blvd, Freehold New Jersey 07728, (US)
LEGAL REPRESENTATIVE:
Warcoin, Jacques et al (19071), Cabinet Regimbeau 26, avenue Kleber, F-75116 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 186576 A2 860702 (Basic)
EP 186576 A3 890125
EP 186576 B1 920722
APPLICATION (CC, No, Date): EP 85402472 851212;
PRIORITY (CC, No, Date): US 684401 841220
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-017/10; A61K-039/02; A61K-039/40; A61K-039/116;

ABSTRACT EP 186576 A2
Covalently-modified neutral bacterial polysaccharides, stable covalent conjugates of such polysaccharides and immunogenic proteins, and methods of preparing such polysaccharides and conjugates.
Covalently-modified neutral bacterial polysaccharides; covalent conjugates of such polysaccharides linked by a bigeneric spacer, with immunogenic bacterial membrane or other proteins, which conjugates are useful components of bacterial vaccines; and methods of preparing such polysaccharides and conjugates.
ABSTRACT WORD COUNT: 60

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1090
CLAIMS B	(German)	EPBBF1	1061
CLAIMS B	(French)	EPBBF1	1274
SPEC B	(English)	EPBBF1	8704
Total word count - document A			0
Total word count - document B			12129
Total word count - documents A + B			12129

8/3,AB/22 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0300749 DBR Accession No.: 2003-02533 PATENT
Novel gram-negative bacterial bleb presenting on its surface PorB *outer"** *membrane"** *protein"** from Chlamydia trachomatis or protective antigen from Chlamydia pneumoniae, useful for preventing Chlamydia infection - vector-mediated mutant gene transfer and expression in Chlamydia trachomatis and Chlamydia pneumoniae for bacterium infection recombinat vaccine production
AUTHOR: BERTHET F J; LOBET Y; POOLMAN J; VERLANT V G C L
PATENT ASSIGNEE: SMITHKLINE BEECHAM BIOLOGICALS 2002
PATENT NUMBER: WO 200262380 PATENT DATE: 20020815 WPI ACCESSION NO.: 2002-657510 (200270)
PRIORITY APPLIC. NO.: GB 20013169 APPLIC. DATE: 20010208
NATIONAL APPLIC. NO.: WO 2002EP1356 APPLIC. DATE: 20020208
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A gram-negative bacterial bleb (I) presenting on its surface the PorB outer membrane protein from

Chlamydia trachomatis, or a protective antigen from C. pneumoniae, is new. DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a vaccine composition (II) comprising (I) and a pharmaceutically suitable excipient or carrier. WIDER DISCLOSURE - (1) a bacterial strain capable of producing (I); (2) a preparation of membrane vesicles obtained from the strain of (1); and (3) a sterile, homogeneous preparation of membrane vesicles obtainable by passing the membrane vesicle from the above mentioned strain through a 0.22 microm membrane. BIOTECHNOLOGY - Preferred Bleb: (I) further presents on its surface the PmpG and MOMP (from one or more serovars) outer membrane proteins from C. trachomatis. (I) presents on its surface both the PorB and MOMP, both MOMP and one or more Pmp, both PorB and one or more Pmp, both the PorB and Nptl, both Nptl and one or more Pmp, or both Nptl and MOMP outer proteins membrane proteins from C. pneumoniae. (I) is a gonococcal or meningococcal bleb which has been derived from a gonococcal or meningococcal strain which has been modified to upregulate one or more protective gonococcal or meningococcal outer membrane antigens, or which has been modified to downregulate one or more immunodominant variable or non-protective gonococcal or meningococcal outer membrane antigens. (I) is derived from a strain which has a detoxified lipid A portion of bacterial lipopolysaccharide (LPS), due to the strain having been engineered to reduce or switch off expression of one or more genes selected from htrB, msbB and lpxK, or due to the strain having been engineered to express at a higher level one or more genes selected from pmrA, pmrB, pmrE and pmrF. Preferred Vaccine: (II) additionally comprises a mucosal adjuvant. ACTIVITY - Antibacterial. No biological data is given. MECHANISM OF ACTION - Vaccine (claimed). USE - (II) is useful for preventing C. trachomatis or C. pneumoniae infection in a host (claimed). ADMINISTRATION - (II) is administered by mucosal, intranasal, oral or intravaginal route (claimed). (II) is administered at a dose of 1-100, preferably 5-25 microg. EXAMPLE - Isolation and purification of blebs from meningococci devoid of capsular polysaccharide was as follows. Cell paste was suspended in 211 ml of 0.1 M Tris-Cl buffer pH 8.6 containing 10 mM ethylenediaminetetraacetic acid (EDTA) and 0.5 % sodium deoxycholate (DOC). The ratio of buffer to biomass was be 5/1 (V/W). The biomass was extracted by magnetic stirring for 30 minutes at room temperature. Total extract was then centrifuged at 20000 g for 30 minutes at 4 degrees C, and the pellet was discarded. The supernatant was ultracentrifuged at 125000 g for 2 hours at 4 degrees C in order to concentrate vesicles, and the supernatant was discarded. The pellet was gently suspended in 25 sucrose. After a second ultracentrifugation step at 125000 g for 2 hours at 4 degrees C, vesicles were gently suspended in 44 ml of 3 % sucrose and stored at 4 degrees C. All solutions used for bleb extraction and purification contained 0.01 % thiomersalate. This procedure yielded protein preparations highly enriched in outer-membrane proteins. (75 pages)

8/3,AB/23 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0290223 DBR Accession No.: 2002-12070 PATENT
Vaccine for protecting host against disease caused by Bordetella pertussis, Haemophilus influenzae, hepatitis B virus, has conjugate of *capsular"** *polysaccharide"** of H. influenzae and two or more *bacterial"** *polysaccharides"** - Neisseria *meningitidis"** antigen,

tetanus *toxoid"**, diphtheria *toxoid"**, hepatitis B virus surface antigen, recombinant diphtheria toxin carrier protein conjugation for vaccine and infection therapy

AUTHOR: BOUTRIAU D; CAPIAU C; DESMONS P M; LEMOINE D; POOLMAN J
PATENT ASSIGNEE: SMITHKLINE BEECHAM BIOLOGICALS 2002

PATENT NUMBER: WO 200200249 PATENT DATE: 20020103 WPI ACCESSION NO.: 2002-280437 (200232)
PRIORITY APPLIC. NO.: GB 20018364 APPLIC. DATE: 20010403
NATIONAL APPLIC. NO.: WO 2001EP7288 APPLIC. DATE: 20010627
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - A multi-valent immunogenic composition (I), comprising conjugate of a carrier protein and capsular polysaccharide (CP) of Haemophilus influenzae type B (HiB) and also comprises 2 or more bacterial polysaccharides capable of conferring protection to a host against infection by bacteria from which they are derived, where HiB CP conjugate is not adsorbed onto an aluminum adjuvant salt, is new. DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for (I) comprising either killed whole-cell Bordetella pertussis (Pw), or two or more acellular pertussis components, tetanus toxoid (TT), diphtheria toxoid (DT), hepatitis B surface antigen (HepB), a conjugate of a carrier protein and the capsular polysaccharide of HiB (where the amount of conjugate per 0.5 ml dose of bulk vaccine is 1-8 micro-g and the immunogenicity of the conjugate is equivalent or improved over such compositions comprising larger amounts of conjugate), and one or more conjugates of a carrier protein and a capsular polysaccharide of a bacterium such as Neisseria meningitidis type A and C. BIOTECHNOLOGY - Preparation: (I) is produced by mixing together the individual components. Preferred Composition: (I) comprises more than 7 further bacterial polysaccharides, preferably pneumococcal CP. None of the polysaccharides in the composition are adsorbed onto an aluminum adjuvant salt. The bacterial CP are N. meningitidis serogroup A CP (MenA), MenC, MenY or MenW, Streptococcus pneumoniae serotype 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F or 33F CP, Group B Streptococcus group I, II, III, IV or V CP, Staphylococcus aureus type 5 or 8, Vi polysaccharide from Salmonella typhi, N. meningitidis lipopolysaccharide (LPS), M. catarrhalis LPS and H. influenzae LPS. The bacterial CP are conjugated to a carrier protein such as TT, DT, CRM197, recombinant diphtheria toxin, OMPC from N.meningitidis, pneumolysin from S. pneumoniae and protein D from H. influenzae. The CP of HiB and the further polysaccharides are not all conjugated to the same carrier, CRM197. (I) further comprises killed, attenuated hepatitis A virus or inactivated polio virus. (I) also comprises aluminum salts as adjuvant. ACTIVITY - Antibiotic; Virucide. MECHANISM OF ACTION - Vaccine. Study MenAC-HiB 001 evaluated the immunogenicity, reactogenicity and safety induced by MenC-HiB and MenAC-HiB (adsorbed and unadsorbed) given as a three-dose primary vaccination in infants. The study was a phase II, randomized study and included five study groups. The formulations that were evaluated were a lyophilized plain and adsorbed formulation of Men AC-HiB and a plain formulation of MenC-HiB. These three formulations were administered to the 3 first study groups of infants at 3, 4 and 5 months of age. Tritanrix-HepB (RTM) (DT-TT-Pw-HepB vaccine) was given concomitantly (as a separate injection) to these three groups. The plain formulation of Men AC-HiB was also reconstituted within a liquid diphtheria, tetanus, whole-cell pertussis, hepatitis B combined vaccine (Tritanrix-HepB) (RTM) and administered as a single injection to the fourth study group of infants at 3, 4 and 5 months of age. The fifth group (control) was administered

Tritanrix-HepB (RTM)-HiB vaccine at 3, 4 and 5 months of age. The results showed that each formulation that was evaluated induced a good immune response against each antigen (antibodies against meningococcal groups A and C, poly-ribosyl-phosphate (the capsular polysaccharide of HiB), diphtheria toxin, TT, Pw and hepatitis B were measured). Each vaccine formulation was well tolerated. USE - (I) is useful as a medicament, and in the manufacture of a medicament for treating or preventing diseases caused by infection by H. influenzae, or Bordetella pertussis, Clostridium tetani, Corynebacterium diphtheriae, hepatitis B virus, H. influenzae and N. meningitidis and also for immunizing a human host against disease caused by the above pathogens (claimed). ADMINISTRATION - The amount of conjugate per 0.5 ml dose of bulk vaccine is 3-6, preferably 5 microg (claimed). Administered by intramuscular, intraperitoneal, intradermal, subcutaneous, mucosal or oral route. ADVANTAGE - (I) is formulated as a vaccine for in vivo administration to the host, where the individual components of the composition are formulated such that the immunogenicity of individual components is not impaired by other individual components of the composition, and (I) confers an antibody titer superior to the criterion for seroprotection for each antigenic component for an acceptable percentage of human subject. (All claimed). The new combination vaccine formulation minimizes the number of immunizations required to confer protection against multiple pathogens, to lower administration costs, and to increase acceptance and coverage rates. EXAMPLE - Unadjuvanted Neisseria meningitidis serogroup A capsular polysaccharide (MenA)-MenC-Haemophilus influenzae type B (HiB) was prepared. MenA and MenC capsular polysaccharide conjugated onto protein D and HiB conjugated onto tetanus toxoid were mixed together in an amount of 5 micro-g of each polysaccharide in each conjugate per 0.5 ml human dose. The pH was adjusted to 6.1, and was lyophilized in the presence of sucrose.(31 pages)

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Set     Items   Description
S9          0   AU=(RYALL, R? OR RYALL R?) AND S1
? log y
       09apr03 09:34:53 User219783 Session D1929.2
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-Author

Devi, S.
10/054638

key terms

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     (FILE 'REGISTRY' ENTERED AT 09:54:23 ON 09 APR 2003)
                E DIPTHTHERIA TOXIOD/CN 5
                E TOXOID/CN
L7            2 S E4-E5
                E CRM 197/CN 5
                E ALUMINUM HYDROXIDE/CN 5
L8            7 S E3-E10
                E ALUMINUM PHOSPHATE/CN 5
L9           14 S E3-E4 OR E6-E19
L10          21 S L8 OR L9

     FILE 'HCAPLUS' ENTERED AT 09:56:26 ON 09 APR 2003
L7            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("TOXOID, DIPHTHERIA
                (CORYNEBACTERIUM DIPHTHERIAE)"/CN OR "TOXOID, TETANUS"/CN
                )
L8            7 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("ALUMINUM HYDROXIDE"/C
                N OR "ALUMINUM HYDROXIDE (AL(18OH)3)"/CN OR "ALUMINUM
                HYDROXIDE (AL(OD))"/CN OR "ALUMINUM HYDROXIDE (AL(OD)2)"/
                CN OR "ALUMINUM HYDROXIDE (AL(OD)3)"/CN OR "ALUMINUM
                HYDROXIDE (AL(OH))"/CN OR "ALUMINUM HYDROXIDE (AL(OH)2)"/
                CN OR "ALUMINUM HYDROXIDE (AL(OH)3)"/CN)
L9           14 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("ALUMINUM PHOSPHATE"/C
                N OR "ALUMINUM PHOSPHATE (1:1)"/CN) OR ("ALUMINUM
                PHOSPHATE (1:3)"/CN OR "ALUMINUM PHOSPHATE (AL(H2PO4)3)"/
                CN OR "ALUMINUM PHOSPHATE (AL(PO3)3)"/CN OR "ALUMINUM
                PHOSPHATE (AL(PO4))"/CN OR "ALUMINUM PHOSPHATE (AL0.5(PO4
                )0.5)"/CN OR "ALUMINUM PHOSPHATE (AL2(HPO4)3)"/CN OR
                "ALUMINUM PHOSPHATE (AL2(OH)3(PO4))"/CN OR "ALUMINUM
                PHOSPHATE (AL2O3(P2O5)5)"/CN OR "ALUMINUM PHOSPHATE
                (AL2P6O18)"/CN OR "ALUMINUM PHOSPHATE (AL3(OH)3(PO4)2)"/C
                N OR "ALUMINUM PHOSPHATE (AL3(PO4)(OH)6)"/CN OR "ALUMINUM
                 PHOSPHATE (AL4(P4O12)3)"/CN OR "ALUMINUM PHOSPHATE
                (AL4P10O31)"/CN OR "ALUMINUM PHOSPHATE (ALH2P3O10)"/CN)
L10          21 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L9
L11         402 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (MENINGITID? OR
                MENINGOCOCC? OR MENB OR MENC OR MENA OR MENY OR MEN(3A)(A
                 OR B OR C OR Y OR W135 OR W 135)) AND (CPS OR CAPSUL?(S)
                (POLYSACCHARID? OR POLY SACCHARID?))
L12         113 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND (L7 OR TOXOID
                OR TT OR DT OR OMP OR OUTER MEMBRAN? PROTEIN OR CRM197
                OR CRM(2W)197)
L13          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 AND (L10 OR (AL OR
                ALUMIN?)(W)(OH OR HYDROXIDE OR PHOSPHATE OR PO##) OR
                ALUM OR ALHYDROGEL OR ALHYDRO GEL OR ALOH# OR ALPO##)

L13  ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:76644  HCAPLUS
DOCUMENT NUMBER:          138:121627
TITLE:                    Purification of bacterial capsular
                          polysaccharide for use in combination
                          vaccines
INVENTOR(S):              Costantino, Paolo
PATENT ASSIGNEE(S):       Chiron S.P.A., Italy
SOURCE:                   PCT Int. Appl., 49 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
```

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007985	A2	20030130	WO 2002-IB3191	20020620

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003009869	A1	20030206	WO 2002-IB3495	20020726

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	GB 2001-15176	A	20010620
	GB 2001-18249	A	20010726
	WO 2002-IB3191	W	20020620

AB The invention provides a process for purifying a bacterial **capsular polysaccharide**, comprising the steps of (a) pptn. of said **polysaccharide**, followed by (b) solubilization of the pptd. **polysaccharide** using ethanol. CTAB can be used for step (a). The material obtained, preferably following hydrolysis and sizing, can be conjugated to a carrier protein and formulated as a vaccine. Also, in vaccines comprising saccharides from the serogroups A and C, the invention provides that the ratio (wt./wt.) of **MenA** saccharide : **MenC** saccharide is >1.

IT **7784-30-7, Aluminum phosphate**
21645-51-2, Aluminum hydroxide,
biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(purifn. of Neisseria **meningitidis capsular polysaccharide** for use in combination vaccines)

L13 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:574960 HCAPLUS
DOCUMENT NUMBER: 137:124195
TITLE: Multivalent **meningococcal** polysaccharide-protein conjugate vaccine
INVENTOR(S): Ryall, Robert P.
PATENT ASSIGNEE(S): Aventis Pasteur, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058737	A2	20020801	WO 2002-US1963	20020122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-263435P P 20010123

AB The author discloses a combined vaccine that offers broad protection against **meningococcal** disease caused by the pathogenic bacterial Neisseria **meningitidis**. The vaccine is comprised of four distinct polysaccharide-protein conjugates that are formulated as a single dose of vaccine. Purified **capsular polysaccharides** from Neisseria **meningitidis** serogroups A, C, W-135, and Y are chem. activated and selectively attached to a carrier protein by a covalent chem. bond, forming **polysaccharide**-protein conjugates capable of eliciting long-lasting immunity to a variety of N. **meningitidis** strains in children as well as adults.

IT **7784-30-7, Aluminum phosphate**
21645-51-2, Aluminum hydroxide,
biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as adjuvant for multivalent vaccine of carrier protein conjugates with **meningococcal capsular polysaccharides**)

L13 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:520216 HCAPLUS
DOCUMENT NUMBER: 136:230824
TITLE: Modulation of the serological response to **meningococcal** polysaccharides by cytokines
AUTHOR(S): Cortes-Castillo, M. d. l. A.; Thorpe, R.; Corbel, M. J.
CORPORATE SOURCE: Division of Bacteriology, National Institute for Biological Standards and Control, Hertfordshire, EN6 3QG, UK
SOURCE: Vaccine (2001), 19(30), 4194-4203
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Meningococcal** A and C but not B **capsular polysaccharides** stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old

CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the polysaccharides were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C polysaccharides with diphtheria mutant protein but exerted a minimal effect on the IgG response to B polysaccharide complexed with **aluminum hydroxide** and **outer membrane proteins**. The stimulatory effect of IL-2 on the antibody responses to the polysaccharide antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/+) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C polysaccharide conjugate and was transferable with T-lymphocytes from primed animals.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:688113 HCAPLUS
DOCUMENT NUMBER: 133:265640
TITLE: Bacterial polysaccharide antigen vaccine
INVENTOR(S): Capiau, Carine; Deschamps, Marguerite; Desmons, Pierre Michel; Laferriere, Craig Antony Joseph; Poolman, Jan; Prieels, Jean-paul
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056360	A2	20000928	WO 2000-EP2468	20000317
WO 2000056360	A3	20010125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 513840	A	20010928	NZ 2000-513840	20000317
NZ 513841	A	20010928	NZ 2000-513841	20000317
EP 1163000	A2	20011219	EP 2000-912626	20000317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009163	A	20011226	BR 2000-9163	20000317
AU 750913	B2	20020801	AU 2000-34307	20000317
JP 2002540075	T2	20021126	JP 2000-606264	20000317

NZ 513842	A	20010928	NZ 2001-513842		20010317
NO 2001004325	A	20011114	NO 2001-4325		20010905
PRIORITY APPLN. INFO.:			GB 1999-6437	A	19990319
			GB 1999-9077	A	19990420
			GB 1999-9466	A	19990423
			GB 1999-16677	A	19990715
			WO 2000-EP2468	W	20000317

AB The present invention relates to the field of bacterial polysaccharide antigen vaccines. In particular, the present invention relates to bacterial polysaccharides conjugated to protein D from H. influenzae.

IT **7784-30-7, Aluminum phosphate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bacterial polysaccharide antigen vaccine)

L13 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:688111 HCAPLUS
DOCUMENT NUMBER: 133:265650
TITLE: Vaccine
INVENTOR(S): Capiau, Carine; Deschamps, Marguerite; Desmons, Pierre Michel; Laferriere, Craig Antony Joseph; Poolman, Jan; Prieels, Jean-paul
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056358	A2	20000928	WO 2000-EP2465	20000317
WO 2000056358	A3	20010104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 513840	A	20010928	NZ 2000-513840	20000317
NZ 513841	A	20010928	NZ 2000-513841	20000317
EP 1162998	A2	20011219	EP 2000-910868	20000317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009154	A	20011226	BR 2000-9154	20000317
AU 750788	B2	20020725	AU 2000-32919	20000317
JP 2002539273	T2	20021119	JP 2000-606262	20000317
NZ 513842	A	20010928	NZ 2001-513842	20010317
NO 2001004322	A	20011114	NO 2001-4322	20010905
PRIORITY APPLN. INFO.:			GB 1999-6437	A 19990319
			GB 1999-9077	A 19990420
			GB 1999-9466	A 19990423
			GB 1999-16677	A 19990715
			WO 2000-EP2465	W 20000317

AB The present invention relates to the field of bacterial polysaccharide antigen vaccines. In particular the present invention relates to specific advantageous pneumococcal polysaccharide conjugates adjuvanted with 3D-MPL and substantially devoid of aluminum-based adjuvant.

IT **7784-30-7, Aluminum phosphate**
RL: REM (Removal or disposal); PROC (Process)
(devoid; bacterial polysaccharide antigen vaccines for preventing pneumonia in elderly)

L13 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:441652 HCAPLUS
DOCUMENT NUMBER: 133:72937
TITLE: Improved recombinant hepatitis B surface antigen
INVENTOR(S): Zhao, Qinjian; Sitrin, Robert; Abraham, Dicky G.; Gervais, David P.; Giminez, Juan
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037104	A1	20000629	WO 1999-US30770	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2355680	AA	20000629	CA 1999-2355680	19991222
EP 1140155	A1	20011010	EP 1999-966613	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532116	T2	20021002	JP 2000-589214	19991222

PRIORITY APPLN. INFO.: US 1998-113400P P 19981223
WO 1999-US30770 W 19991222

AB The present invention provides an improved rHBsAg that exhibits a higher antigenicity and immunogenicity than that previously known in the art. A method of making the improved rHBsAg is also provided. The improved HBsAg is used to provide vaccines with lower amts. of active ingredient, vaccines with higher immunogenicity and combination vaccines which produce and protective immunization against infection by hepatitis B virus and other infectious agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:626070 HCAPLUS
DOCUMENT NUMBER: 131:262583
TITLE: Haemophilus influenzae B-DTPa combination

vaccine
INVENTOR(S): Artois, Claude; De Heyder, Koen; Desmons, Pierre; Garcon, Nathalie; Mainil, Roland
PATENT ASSIGNEE(S): SmithKline Beecham Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948525	A1	19990930	WO 1999-EP1959	19990322
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2325436	AA	19990930	CA 1999-2325436	19990322
AU 9934172	A1	19991018	AU 1999-34172	19990322
AU 735619	B2	20010712		
BR 9909037	A	20001205	BR 1999-9037	19990322
EP 1066053	A1	20010110	EP 1999-915692	19990322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
JP 2002507581	T2	20020312	JP 2000-537572	19990322
NZ 506604	A	20030228	NZ 1999-506604	19990322
NO 2000004758	A	20001108	NO 2000-4758	20000922
US 2003022304	A1	20030130	US 2002-217572	20020813

PRIORITY APPLN. INFO.:
GB 1998-6456 A 19980325
WO 1999-EP1959 W 19990322
US 2000-647032 B1 20001031

AB This invention relates to a general method by which either extemporaneously prepd. or liq. Haemophilus influenzae B (Hib)/DTPa combination vaccines can be made in order to avoid Hib interference while being able to maintain the max., stable adsorption of each antigen onto the aluminum-based adjuvant on which it is most immunogenic. In so doing, pertussis antigens in combination vaccines of the present invention are stably retained in their most potent form. Examples are given for the vaccines using **Al hydroxide** or **Al phosphate** as adjuvants.

IT **7784-30-7, Aluminum phosphate**
21645-51-2, Aluminum hydroxide,
biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Haemophilus influenzae B-DTPa combination vaccine)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:529041 HCAPLUS
DOCUMENT NUMBER: 131:175069

TITLE: Pneumococcal and **meningococcal** vaccines formulated with interleukin-12 adsorbed onto mineral suspension
INVENTOR(S): Laposta, Vincent J.; Eldridge, John H.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940936	A2	19990819	WO 1999-US2847	19990210
WO 9940936	A3	19991028		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2320223	AA	19990819	CA 1999-2320223	19990210
AU 9925965	A1	19990830	AU 1999-25965	19990210
BR 9907884	A	20001024	BR 1999-7884	19990210
EP 1053015	A2	20001122	EP 1999-905924	19990210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002502882	T2	20020129	JP 2000-531187	19990210

PRIORITY APPLN. INFO.: US 1998-74528P P 19980212
WO 1999-US2847 W 19990210

AB This invention pertains to vaccine compns. comprising a mixt. of antigen, such as a pneumococcal or **meningococcal** antigen, and interleukin IL-12, which may be adsorbed onto a mineral in suspension. The pneumococcal or **meningococcal** antigen may be conjugated to a carrier mol. These vaccine compns. modulate the protective immune response to the antigen.

IT **7784-30-7, Aluminum phosphate**
21645-51-2, Aluminum hydroxide,
biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pneumococcal and **meningococcal** vaccines formulated with interleukin-12 adsorbed onto mineral suspension)

L13 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:231136 HCAPLUS
DOCUMENT NUMBER: 131:78309
TITLE: Haemophilus influenzae type b conjugate vaccine stability: catalytic depolymerization of PRP in the presence of **aluminum hydroxide**
AUTHOR(S): Sturgess, Annie W.; Rush, Kay; Charbonneau,

Ronald J.; Lee, James I.; West, David J.; Sitrin, Robert D.; Hennessey, John P., Jr.
CORPORATE SOURCE: Bioprocess and Bioanalytical Research, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Vaccine (1999), 17(9-10), 1169-1178
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The structural stability of the Haemophilus influenzae type b (Hib) **capsular polysaccharide**, polyribosylribitolphosphate (PRP) in an **aluminum hydroxide** adsorbed, **polysaccharide**-protein conjugate vaccine was monitored using modifications of an HPLC assay developed by Tsai et al. As applied to products contg. PRP conjugated to the **outer membrane protein** complex (OMPC) from Neisseria **meningitidis**, this assay allows direct measurement of the total PRP content in very complex samples including com. vaccine products. In addn., with the use of a high-speed centrifugation step, the assay can be used to directly quantify any PRP that is not conjugated to the OMPC carrier protein. These results provide evidence of what appears to be a catalytic reaction taking place between the phosphodiester bond of PRP and the **aluminum hydroxide** adjuvant that results in hydrolysis of the PRP polymer into smaller chain lengths and liberation of PRP oligomers from the conjugate particle. The reaction approaches an asymptotic limit after approx. two years at 2-8.degree.C. Clin. studies which span this time period confirm that the modest decrease in conjugated PRP content over time does not impact the overall clin. effectiveness of PRP-OMPC-contg. vaccines.
IT **21645-51-2, Aluminum hydroxide,** biological studies
RL: CAT (Catalyst use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Haemophilus influenzae type b conjugate vaccine stability and catalytic depolymn. of polyribosylribitolphosphate in the presence of **aluminum hydroxide**)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:145259 HCAPLUS
DOCUMENT NUMBER: 126:148484
TITLE: Vaccine composition comprising a polysaccharide conjugate antigen adsorbed onto **aluminum phosphate**
INVENTOR(S): Peetermans, Julien; Hauser, Pierre
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.; Peetermans, Julien; Hauser, Pierre
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700697	A1	19970109	WO 1996-EP2690	19960619
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
CN 1215337	A	19990428	CN 1996-194891	19960604
EP 1090642	A2	20010411	EP 2000-203772	19960604
EP 1090642	A3	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2222455	AA	19970109	CA 1996-2222455	19960619
AU 9663591	A1	19970122	AU 1996-63591	19960619
AU 696338	B2	19980910		
EP 833662	A1	19980408	EP 1996-922871	19960619
EP 833662	B1	20010321		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
CN 1188418	A	19980722	CN 1996-194973	19960619
BR 9609414	A	19990518	BR 1996-9414	19960619
JP 11507935	T2	19990713	JP 1996-503581	19960619
AP 812	A	20000224	AP 1997-1159	19960619
W: GH, GM, KE, LS, MW, SD, SZ, UG, ZW				
EP 1082965	A1	20010314	EP 2000-203874	19960619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
AT 199831	E	20010415	AT 1996-922871	19960619
ES 2157447	T3	20010816	ES 1996-922871	19960619
CZ 288908	B6	20010912	CZ 1997-4189	19960619
IL 122588	A1	20011223	IL 1996-122588	19960619
ZA 9605274	A	19970527	ZA 1996-5274	19960621
TW 467746	B	20011211	TW 1996-85107646	19960625
NO 9706035	A	19980216	NO 1997-6035	19971222
US 2002054884	A1	20020509	US 2001-951657	20010913
US 2002182226	A1	20021205	US 2002-155052	20020523

PRIORITY APPLN. INFO.:		
GB 1995-12827	A	19950623
GB 1995-13443	A	19950701
GB 1995-25657	A	19951215
GB 1996-6032	A	19960322
US 1995-472639	A	19950607
EP 1996-920790	A3	19960604
EP 1996-922871	A3	19960619
WO 1996-EP2690	W	19960619
GB 1996-9513443	A	19960701
US 1998-983271	B1	19980211
US 2000-522234	A1	20000309
US 2001-951657	B1	20010913

AB The invention relates to a vaccine formulation for the prevention of Hemophilus influenzae Type B (Hib) infections and where the antigen is adsorbed onto **aluminum phosphate**. The antigen is a **capsular polysaccharide** from H. influenzae B conjugate with a carrier protein. The carrier protein is Diphtheria **toxoid**, Diphtheria **CRM197** protein, **meningococcal outer membrane**

protein or Tetanus **toxoid**. The invention also relates to a multivalent vaccine.

IT **7784-30-7, Aluminum phosphate**
RL: MOA (Modifier or additive use); USES (Uses)
(vaccine compn. comprising polysaccharide conjugate antigen adsorbed onto)

L13 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:548530 HCAPLUS
DOCUMENT NUMBER: 125:177440
TITLE: Immunogenic conjugate molecules
INVENTOR(S): Yang, Yan-Ping; Kandil, Ali; Gisonni, Lucy; Fahim, Raafat E. F.; Klein, Michel H.
PATENT ASSIGNEE(S): Connaught Laboratories Limited, Can.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9621465	A2	19960718	WO 1996-CA7	19960105
WO 9621465	A3	19961010		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN				
US 5681570	A	19971028	US 1995-371965	19950112
US 6177085	B1	20010123	US 1995-467884	19950606
US 6329512	B1	20011211	US 1995-467883	19950606
CA 2210139	AA	19960718	CA 1996-2210139	19960105
AU 9643254	A1	19960731	AU 1996-43254	19960105
EP 805691	A2	19971112	EP 1996-900066	19960105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				

PRIORITY APPLN. INFO.: US 1995-371965 A2 19950112
WO 1996-CA7 W 19960105

AB Immunogenic conjugate mols. comprising at least a portion of a **capsular polysaccharide** of a Streptococcus strain linked to at least a portion of an **outer membrane protein** of a Haemophilus strain are provided in which the immunogenicity of the **capsular polysaccharide** is increased. Particularly **capsular polysaccharide** from Streptococcus pneumoniae are linked to an **outer membrane protein** of a Haemophilus influenzae strain, which protein may be the P1, P2 or particularly the P6 **outer membrane protein**. Conjugate mols. comprising the P6 protein linked to a **capsular polysaccharide** from an encapsulated pathogen other than Streptococcus are also described, in which the immunogenicity of the **capsular polysaccharide** is enhanced. Such conjugate mols. may be incorporated into immunogenic compns. for protecting a host against disease caused by the Streptococcus strain

and preferably also the Haemophilus strain. The conjugate mols. and antibodies specific for the **capsular polysaccharide** or specific for the **outer membrane protein** may be employed in diagnostic procedures and kits. A process for individually isolating P1, P2 and P6 **outer membrane proteins** from a Haemophilus strain is also provided.

IT **7784-30-7, Aluminum phosphate**
21645-51-2, Aluminum hydroxide,
biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunoconjugates based on polysaccharide from Streptococcus and **outer membrane protein** from Haemophilus)

L13 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:653768 HCAPLUS
DOCUMENT NUMBER: 115:253768
TITLE: Human IgA1 blockade of IgG-initiated lysis of Neisseria **meningitidis** is a function of antigen-binding fragment binding to the **polysaccharide capsule**
AUTHOR(S): Jarvis, Gary A.; Griffiss, J. McLeod
CORPORATE SOURCE: Cent. Immunochem., Univ. California, San Francisco, CA, 94121, USA
SOURCE: Journal of Immunology (1991), 147(6), 1962-7
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have recently shown that human IgA1 can initiate lysis of group C N. **meningitidis** via the classical complement pathway when bound to specific **outer membrane proteins**, but that IgA1 can also function as a blocking antibody when bound to the **polysaccharide capsule** of **meningococci**. In this report, the blockade was further characterized by examg. the effect of IgA1 on IgG-initiated immune lysis of group C **meningococci**. IgG and monomeric IgA1 were purified from either convalescent group C **meningococcal** case sera or tetravalent (A, C, Y, W135) polysaccharide vaccinate sera. In the absence of IgA1, IgG initiated complete lysis (>99%) of strains 118V (C:P3,4:L2,4) 126E (C:P3:L1,8), and 35E (C:P5:L2). Addn. of IgA1 to the bactericidal reaction mixt. completely blocked the lytic function of IgG. Removal of the Fc portion of IgA2 with either pepsin or IgA1 protease did not affect blockade. Both the F(ab')2 and Fab derivs. of IgA1 blocked lysis quant. as well as intact IgA1. The Fc fragment produced by IgA1 protease cleavage neither increased nor decreased Fab-mediated blockade. IgA1 and its Fab and F(ab')2 fragments blocked IgG-initiated lysis via either the classical pathway in factor B-depleted and in properdin-deficient serum, the alternative pathway in MgEGTA-chelated serum, or both pathways combined. Absorption of the IgA1 and IgG with **alum** -bound group C **polysaccharide** completely removed blocking and lytic activity, resp., indicating that both the blocking IgA1 and the lytic IgG were specific for the group C **capsule**. Blocking by IgA1 was a linear function of the polysaccharide antigens-binding capacity (ABC) ratio of blocking IgA1 to lytic IgG. Complete blockade was obsd. at an ABC ratio of 5.5. At ABC ratios of 3.3 and 4.4, IgA1 affected significant blockade whether added

previous to, concurrent with, or subsequent to sensitization of the organisms with IgG. With the use of a C **polysaccharide** ELISA, the binding of IgA1 to the group C **capsule** in the presence of IgG exhibited pos. cooperativity and therefore that blockade was independent of the ability of IgA1 to directly compete with IgG for binding to epitopes within the group C **capsule** . IgA2, when bound to the group C **polysaccharide** **capsule**, can block IgG-initiated lysis group C meningogocci through either the classical or the alternative pathway before or after the organism is exposed to IgG, and that blockade is an Fc-independent event.

L13 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:551114 HCAPLUS
DOCUMENT NUMBER: 105:151114
TITLE: Class 1/3 **outer membrane** **protein** vaccine against group B, type 15, subtype 16 **meningococci**
AUTHOR(S): Poolman, J. T.; Beuvery, E. C.; Hopman, Carla T. P.; Witvliet, M. H.; Timmermans, H. A. M.; Teerlink, T.; Zanen, H. C.
CORPORATE SOURCE: Lab. Med. Microbiol., Univ. Amsterdam, Amsterdam, 1105 AZ, Neth.
SOURCE: Developments in Biological Standardization (1986), 63(Use Stand. Chem. Defined Antigens), 147-52
CODEN: DVBSA3; ISSN: 0301-5149
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neisseria **meningitidis** **Capsular** **polysaccharides** and **outer membrane** **proteins** have been incorporated in vaccines and the potential of these vaccines has been evaluated in man. Polysaccharides are the most attractive candidates for a vaccine against group A and C **meningococci**, whereas **outer** **membrane proteins** may have a potential for a vaccine against group B **meningococci**. This paper described the characteristics of the 5 classes of **outer** **membrane proteins** of group B **meningococci** and the protective (bactericidal) activity of monoclonal antibodies against class 1 and 2 or 3 **outer membrane** **proteins**. Monoclonal antibodies against class 1 **outer membrane proteins** were bactericidal irresp. of the growth conditions of the bacterium. On the other hand, these conditions influenced the bactericidal activity of monoclonal antibodies against class 2 or 3 **outer** **membrane proteins**. Thus, class 1 **outer** **membrane protein** is an attractive component of a vaccine. The M. Blake and E. Gotschlich procedure for the isolation of gonococcal **outer membrane protein** II was adapted for the isolation of a combination of class 1 and 3 **outer membrane proteins** from group B, type 15 **meningococci**. The combination of both **outer membrane proteins** was adsorbed to **AlPO4** i the presence of the detergent Zwittergent 3-14. The vaccine was injected into mice. The antibodies were strongly bactericidal, and Western blot anal. indicated that both **outer membrane proteins** induced

antibodies. The vaccine may have a potential to combat an epidemic caused by group B, type 15 **meningococci**.

L13 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:4250 HCAPLUS
DOCUMENT NUMBER: 102:4250
TITLE: Development of a Neisseria **meningitidis** group B serotype 2b protein vaccine and evaluation in a mouse model
AUTHOR(S): Wang, Li Ya; Frasch, Carl E.
CORPORATE SOURCE: Off. Biol., Cent. Drugs Biol., Bethesda, MD, 20205, USA
SOURCE: Infection and Immunity (1984), 46(2), 408-14
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although serotype 2 remains the predominant cause of group B N. **meningitidis** disease in many parts of the world, most cases of this disease are now due to serotype 2b rather than 2a. For this reason, the serotype 2a vaccine method of C. E. Frasch and M. S. Peppler (1982) was adapted to the prodn. of a serotype 2b protein vaccine. A spontaneously occurring nonencapsulated mutant of the group B serotype 2b strain 3006 was obtained by selection on group B antiserum agar. Serotype 2b **outer membrane protein** vaccines were prepd. with less than 1% lipopolysaccharide contamination. The immunogenicity of these vaccines was evaluated in mice in the presence and absence of **meningococcal** group B and group C **capsular polysaccharides**. The group B and C polysaccharides equally potentiated the antibody response to the serotype 2b protein. Addn. of **aluminum hydroxide** or **aluminum phosphate** markedly improved the antibody response to the serotype 2b protein, but **aluminum hydroxide** -adjuvanted vaccines consistently elicited higher antibody levels. **Aluminum hydroxide**-adsorbed serotype 2a and 2b protein vaccines were evaluated for induction of cross-protective bactericidal antibodies. The 2a vaccines were 2a specific, whereas the 2b vaccines elicited antibodies strongly bactericidal for both 2a and 2b **meningococcal** strains and protected against bacteremia in a mouse model. It may therefore be possible to provide protection against both 2a and 2b disease by using an **aluminum hydroxide**-adsorbed protein vaccine contg. a single serotype 2 protein component.
IT **7784-30-7 21645-51-2**, biological studies
RL: BIOL (Biological study)
(as immune adjuvant, antibody response to Neisseria **meningitidis** group B serotype 2b protein vaccine response to)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JAPIO, JICST-EPLUS, PHIC, PHIN, TOXCENTER' ENTERED AT 10:02:48 ON 09 APR 2003)
L14 31 S L13
L15 18 DUP REM L14 (13 DUPLICATES REMOVED)

L15 ANSWER 1 OF 18 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-239273 [23] WPIDS
DOC. NO. CPI: C2003-061372
TITLE: Purification of bacterial **capsular**

polysaccharides, useful in vaccines, particularly against Neisseria **meningitidis**, by precipitation then resolubilization in alcohol.

DERWENT CLASS: B04 D16
INVENTOR(S): COSTANTINO, P
PATENT ASSIGNEE(S): (CHIR-N) CHIRON SPA
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003007985	A2	20030130	(200323)*	EN	49

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003007985	A2	WO 2002-IB3191	20020620

PRIORITY APPLN. INFO: GB 2001-15176 20010620
AN 2003-239273 [23] WPIDS
AB WO2003007985 A UPAB: 20030407
NOVELTY - Purification of bacterial **capsular polysaccharides** (I) by precipitation of (I) then solubilization of the precipitate with an alcohol, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) vaccine made from (I) purified this way;

(2) solubilization of precipitated (I) using ethanol;

(3) vaccine comprising (I) from at least serogroups A and C of Neisseria **meningitidis** where the weight ratio of A:C saccharides is over 1;

(4) vaccine comprising a synergistic combination of (I) from N. **meningitidis** serogroup W135 and (I) from at least one other serogroup;

(5) vaccine containing a mixture of (I) antigens from at least 2 serogroups, one being W135, in which the immunogenicity of the W135 antigen is greater than when it is used alone;

(6) vaccine containing (I) from at least of the serogroups A, C, W135 and Y conjugated to at least one carrier protein;

(7) vaccine containing (I) from at least of the serogroups A, C, W135 and Y where (I) are oligosaccharides;

(8) kit containing (I) of serogroup A in lyophilized form and (I) from at least one of serogroups C, W135 and Y in liquid form;

(9) kit containing (I) of serogroup A in lyophilized form and additional antigens in liquid form; and

(10) immunogenic composition containing serogroup A or C oligosaccharides and **aluminum phosphate** and phosphate buffer or **aluminum hydroxide** and

histidine buffer.

ACTIVITY - Antibacterial; Antiinflammatory.

Mice were injected with a combination vaccine containing 2 micro g each of oligosaccharides from N. **meningitidis** serotypes A, C, W135 and Y, formulated with **aluminum phosphate**. The mean antibody titers, measured by enzyme-linked immunosorbent assay, were 132, 582, 143 and 247 for the four serotypes.

MECHANISM OF ACTION - Vaccine.

USE - (I) are used to produced vaccines for treatment or prevention of infections by Neisseria **meningitidis**, Haemophilus influenzae or Streptococcus pneumoniae, especially meningitis.

ADVANTAGE - The two-step precipitation and solubilization process is quicker and simpler than known methods of purification. Vaccines containing (I) from different serogroups of Neisseria **meningitidis** may show a synergistic increase in immunogenicity.

Dwg.0/19

L15 ANSWER 2 OF 18 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-657464 [70] WPIDS
DOC. NO. CPI: C2002-184454
TITLE: New multivalent vaccine comprises protein-**polysaccharide** conjugates comprising a **capsular polysaccharide** from 2 or more serogroup of Neiserria **meningitidis**, useful for treating or preventing **meningococcal** infections.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): RYALL, R P
PATENT ASSIGNEE(S): (AVET) AVENTIS PASTEUR
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002058737	A2	20020801	(200270)*	EN	29

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002058737	A2	WO 2002-US1963	20020122

PRIORITY APPLN. INFO: US 2001-263435P 20010123
AN 2002-657464 [70] WPIDS
AB WO 200258737 A UPAB: 20021031
NOVELTY - An immunological composition comprising 2-4 distinct protein-**polysaccharide** conjugates, each comprising a

capsular polysaccharide from 2 or more serogroup of Neiserria **meningitidis** conjugated to one or more carrier protein(s), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of inducing immunological response to **capsular polysaccharide** of N. **meningitidis**, or protecting a human or animal susceptible to infection by N. **meningitidis** , comprises administering the immunological composition described above.

ACTIVITY - Antibacterial; Immunostimulant.

MECHANISM OF ACTION - Vaccine.

USE - The immunological composition is useful as a multivalent vaccine for treating **meningococcal** infection (claimed) and as research tools for studying the biological pathways and processes involved in T-dependent-like immune responses to N. **meningitides** antigens.

ADVANTAGE - Existing vaccines based on **meningococcal** polysaccharide are of limited use in young children and do no provide long lasting protection in adults. The only **meningococcal** vaccine capable of eliciting long lasting protection in all groups at risk for **meningococcal** infection does not provide protection against infection by other serogroups. The new multivalent vaccine, which is capable of conferring broad, long-lived protection against **meningococcal** disease in children and adults at risk for **meningococcal** infection, overcomes those problems encountered with existing vaccines.

Dwg.0/0

L15 ANSWER 3 OF 18 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER:	2001-138654 [14] WPIDS
CROSS REFERENCE:	2002-188688 [24]
DOC. NO. CPI:	C2001-041027
TITLE:	New isolated polynucleotide useful for outer membrane vesicle preparation from Gram-negative bacterial strain for vaccination of microbial infections.
DERWENT CLASS:	B04 D16
INVENTOR(S):	BERTHET, F J; DALEMANS, W L J; DENOEL, P; DEQUESNE, G; FERON, C; LOBET, Y; POOLMAN, J; THIRY, G; THONNARD, J; VOET, P; DALEMANS, W L; LHONNARD, J
PATENT ASSIGNEE(S):	(SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (SMIK) SMITHKLINE BEECHAM BIOLOGICALS SA
COUNTRY COUNT:	95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001009350	A2	20010208	(200114)*	EN	127
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000068336	A	20010219	(200129)		
NO 2002000506	A	20020402	(200235)		

BR 2000012974 A 20020507 (200238)
CZ 2002000403 A3 20020515 (200241)
EP 1208214 A2 20020529 (200243) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
KR 2002027514 A 20020413 (200267)
HU 2002003056 A2 20021228 (200308)
CN 1377415 A 20021030 (200314)
JP 2003506049 W 20030218 (200315) 189

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001009350	A2	WO 2000-EP7424	20000731
AU 2000068336	A	AU 2000-68336	20000731
NO 2002000506	A	WO 2000-EP7424	20000731
		NO 2002-506	20020131
BR 2000012974	A	BR 2000-12974	20000731
		WO 2000-EP7424	20000731
CZ 2002000403	A3	WO 2000-EP7424	20000731
		CZ 2002-403	20000731
EP 1208214	A2	EP 2000-956369	20000731
		WO 2000-EP7424	20000731
KR 2002027514	A	KR 2002-701441	20020201
HU 2002003056	A2	WO 2000-EP7424	20000731
		HU 2002-3056	20000731
CN 1377415	A	CN 2000-813842	20000731
JP 2003506049	W	WO 2000-EP7424	20000731
		JP 2001-514142	20000731

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000068336	A	Based on	WO 200109350
BR 2000012974	A	Based on	WO 200109350
CZ 2002000403	A3	Based on	WO 200109350
EP 1208214	A2	Based on	WO 200109350
HU 2002003056	A2	Based on	WO 200109350
JP 2003506049	W	Based on	WO 200109350

PRIORITY APPLN. INFO: GB 1999-18319 19990803
AN 2001-138654 [14] WPIDS
CR 2002-188688 [24]
AB WO 200109350 A UPAB: 20030303
NOVELTY - An isolated polynucleotide sequence which hybridizes under highly stringent conditions to at least a 30 nucleotide portion of 80 sequences described in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a genetically-engineered outer membrane vesicle (bleb) preparation from a Gram-negative bacterial strain characterized in that the preparation is obtainable by employing a process comprising:

(a) introducing a heterologous gene, optionally controlled by a strong promoter sequence, into the chromosome by homologous recombination; and

(b) making blebs from the strain;

(2) a vaccine comprising a bleb preparation and a pharmaceutically acceptable excipient;

(3) a vector suitable for performing recombination events;

(4) a modified Gram-negative bacterial strain from which the bleb preparation is made;

(5) an immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell vaccine suitable for paediatric use.

ACTIVITY - Antiviral; Antibacterial; Antifungal.

Animals were immunized three times with 5 micro g of the different OMVs absorbed on **Al**(**OH**)3 on days 0, 14, and 28. Bleedings were done on days 28 and 35, and they were challenged on day 35. The challenge dose was 20 X LD50 (approx. 10 to the power of 7 CFU/mouse). Mortality rate was monitored for 7 days after challenge.

OMVs injected were:

Group1: **Cps**-, PorA+

Group2: **Cps**-, PorA-

Group3: **Cps**-, PorA-, NspA+

Group4: **Cps**-, PorA-, Omp85+

Group5: **Cps**-, PorA-, Hsf+

24 hours after the challenge, there was 100% mortality in the negative control group, while mice immunized with the 5 different OMVs preparations were still alive. Sickness was also monitored during the 7 days and the mice immunized with the NSPA over-expressed blebs appeared to be less sick than the other groups. PorA present in PorA+ blebs is likely to confer extensive protection against infection by the homologous strain. However, protection induced by PorA-up-regulated blebs is likely to be due at least to some extent, to the presence of increased amount of NspA, OMP85 or Hsf.

MECHANISM OF ACTION - Vaccine.

USE - The claimed polynucleotide sequence is used in performing a homologous recombination event within 1000 base pairs upstream of a Gram-negative bacterial chromosomal gene in order to either increase or decrease expression of the gene. The bleb preparation is useful in the manufacture of a medicament for immunizing a human host against a disease caused by infection of one or more of the following: Neisseria **meningitidis**, Neisseria gonorrhoeae, Haemophilus influenza, Moraxella catarrhalis, Pseudomonas aeruginosa, Chlamydia trachomatis, and Chlamydia pneumonia. The invention is useful for immunizing a human host against the diseases caused by the above. The invention also provides immunization against the influenza virus. Immuno-protective and non-toxic Gram-negative bleb, ghost, or killed whole cell vaccines are useful for paediatric use (all claimed).

ADVANTAGE - The vaccine is more immunogenic, less toxic, and safer.

Dwg.0/17

L15 ANSWER 4 OF 18 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2001406624 MEDLINE

DOCUMENT NUMBER: 21351499 PubMed ID: 11457545

TITLE: Modulation of the serological response to **meningococcal** polysaccharides by cytokines.

AUTHOR: Cortes-Castillo M A; Thorpe R; Corbel M J

CORPORATE SOURCE: Division of Bacteriology, National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, EN6 3QG, Hertfordshire, UK.

SOURCE: VACCINE, (2001 Jul 20) 19 (30) 4194-203.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20011001
Last Updated on STN: 20011001
Entered Medline: 20010927

AB **Meningococcal** A and C but not B **capsular polysaccharides** stimulated a low level primary antibody response, predominantly IgM, and no secondary response in 21-day-old CBA/A mice. However, in 56-day-old mice a higher proportion of IgG antibody and a secondary response were produced. When the **polysaccharides** were injected in conjunction with rDNA derived human interleukin 2 (IL-2) the IgG antibody responses were increased in both age groups and memory cells were primed in the younger mice. IL-2 increased significantly the IgG antibody response to conjugates of A and C **polysaccharides** with diphtheria mutant protein but exerted a minimal effect on the IgG response to B **polysaccharide** complexed with **aluminium hydroxide** and **outer membrane proteins**. The stimulatory effect of IL-2 on the antibody responses to the **polysaccharide** antigens was not mediated by T-cells as similar results were obtained in athymic (nu/nu) and thymocompetent (nu/+) mice. However, the response to the A and C oligosaccharide conjugates was T-cell dependent and occurred only in the heterozygotes. In this case the adjuvant effect of IL-2 was seen only in the response to the C **polysaccharide** conjugate and was transferable with T-lymphocytes from primed animals.

L15 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:223198 BIOSIS
DOCUMENT NUMBER: PREV200200223198

TITLE: Stability of Group C **meningococcal** polysaccharide-tetanus **toxoid** conjugate vaccine (NeisVac-C): Correlation of immunochemical and serological analyses of vaccines heated to 100degreeC.

AUTHOR(S): Moore, S. L. (1); Ren, K. (1); Huang, C. H. (1); Fusco, P. C. (1); Michon, F. (1)
CORPORATE SOURCE: (1) Baxter Healthcare Corporation, Columbia, MD USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 339. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Coupling T-cell independent antigens such as the **capsular polysaccharide** (**CPS**) from Group C Neisseria **meningitidis** to a T-cell dependent carrier protein enhances the immune response to such antigens. The potency of these vaccines is dependent on the maintenance of the structural integrity of the

conjugate molecule. Group C **meningococcal polysaccharide**-tetanus **toxoid** (NeisVac-C) conjugate vaccine samples were formulated both in the presence and absence of **Al**(**OH**)3 adjuvant. Samples were then heated in a water bath to 100degreeC for up to 4 hours and tested by a competitive enzyme-linked immunosorbent assay (ELISA) for preservation of the antigenicity of both the **CPS** and protein components of the conjugate. Samples were then further diluted and placed in a mouse potency study to examine 2.0 and 0.1 mug **CPS** doses. Competitive ELISA results indicated that in the presence of **Al**(**OH**)3, there was no significant decrease in the antigenicity of the **CPS** component of NeisVac-CTM, even after heating to 100degreeC for up to four hours. By contrast, in the absence of **Al**(**OH**)3 there was a 10-fold loss of antigenicity of the **CPS** after only 1 hour. The antigenicity of the protein component was drastically reduced after just 5 minutes at 100degreeC in both formulations. Potency studies examining ELISA IgG and serum bactericidal activity of antisera produced by immunization with these vaccines showed only minimal decreases in activity after 4 hours at 100degreeC. Antigenicity results from competitive ELISA closely predicted the immunogenicity results of the mouse potency assay for NeisVac-CTM. The **CPS** component of this vaccine was exceedingly stable under heat stress when adsorbed with **Al**(**OH**)3, showing only marginal losses in immunogenicity while the protein carrier was antigenically altered with heat.

L15 ANSWER 6 OF 18 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-594517 [56] WPIDS
CROSS REFERENCE: 2000-594515 [56]; 2000-594516 [56]; 2000-679550 [66]; 2001-006956 [01]
DOC. NO. CPI: C2000-177617
TITLE: A Streptococcus pneumoniae vaccine for preventing pneumonia and meningitis comprises a polysaccharide antigen conjugated to protein D from Haemophilus influenzae.
DERWENT CLASS: B04 D16
INVENTOR(S): CAPIAU, C; DESCHAMPS, M; DESMONS, P M; LAFERRIERE, C A J; POOLMAN, J; PRIEELS, J; POOLMAN, J P J
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000056360	A2	20000928	(200056)*	EN	77
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000034307	A	20001009	(200103)		
BR 2000009163	A	20011226	(200206)		
EP 1163000	A2	20011219	(200206)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK					

NL PT RO SE SI

CZ	2001003380 A3	20020313	(200223)	
KR	2002000549 A	20020105	(200244)	
HU	2002000367 B	20020528	(200249)	
CN	1351503 A	20020529	(200258)	
AU	750913 B	20020801	(200261)	
ZA	2001007637 A	20020828	(200264)	97
JP	2002540075 W	20021126	(200307)	96

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000056360	A2	WO 2000-EP2468	20000317
AU 2000034307	A	AU 2000-34307	20000317
BR 2000009163	A	BR 2000-9163	20000317
		WO 2000-EP2468	20000317
EP 1163000	A2	EP 2000-912626	20000317
		WO 2000-EP2468	20000317
CZ 2001003380	A3	WO 2000-EP2468	20000317
		CZ 2001-3380	20000317
KR 2002000549	A	WO 2000-EP2468	20000317
		KR 2001-711939	20010919
HU 2002000367	B	WO 2000-EP2468	20000317
		HU 2002-367	20000317
CN 1351503	A	CN 2000-807528	20000317
AU 750913	B	AU 2000-34307	20000317
ZA 2001007637	A	ZA 2001-7637	20010917
JP 2002540075	W	JP 2000-606264	20000317
		WO 2000-EP2468	20000317

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000034307	A	Based on	WO 200056360
BR 2000009163	A	Based on	WO 200056360
EP 1163000	A2	Based on	WO 200056360
CZ 2001003380	A3	Based on	WO 200056360
KR 2002000549	A	Based on	WO 200056360
HU 2002000367	B	Based on	WO 200056360
AU 750913	B	Previous Publ.	AU 200034307
		Based on	WO 200056360
JP 2002540075	W	Based on	WO 200056360

PRIORITY APPLN. INFO: GB 1999-16677 19990715; GB 1999-6437 19990319; GB 1999-9077 19990420; GB 1999-9466 19990423

AN 2000-594517 [56] WPIDS

CR 2000-594515 [56]; 2000-594516 [56]; 2000-679550 [66]; 2001-006956 [01]

AB WO 200056360 A UPAB: 20030129

NOVELTY - A polysaccharide conjugate antigen (I) comprising a polysaccharide antigen derived from a pathogenic bacterium conjugated to protein D (or a fragment) from Haemophilus influenzae, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an immunogenic composition comprising (I);
(2) an immunogenic composition comprising Neisseria **meningitidis** protein D polysaccharide conjugate antigen;
(3) an immunogenic composition comprising Haemophilus influenzae b protein D polysaccharide conjugate antigen;
(4) an immunogenic composition comprising conjugated **capsular polysaccharides** of Streptococcus pneumoniae, Haemophilus influenzae b , **meningococcus** C and **meningococcus** Y, the carrier protein for at least one of the **polysaccharides** is protein D from H. influenzae;
(5) a vaccine comprising (1)-(4); and
(6) a method for producing an immunogenic composition to a pathogenic bacterium comprising:
(a) isolating a polysaccharide antigen from a pathogenic bacterium;
(b) activating the polysaccharide; and
(c) conjugating the polysaccharide to protein D.
ACTIVITY - Antibacterial. No biological data given
MECHANISM OF ACTION - Vaccine.
USE - The bacterial polysaccharide antigen vaccines are used to induce an immune response to Streptococcus pneumoniae and is used to prevent pneumonia, bacteremia, meningitis and acute otitis media.
ADVANTAGE - The conjugation of the antigen to a larger immunogenic protein increases the induced immune response, especially in children less than two years old.
Dwg.0/3

L15 ANSWER 7 OF 18 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1999-580365 [49] WPIDS
DOC. NO. CPI: C1999-168834
TITLE: Reducing interference from Haemophilus polysaccharide component in combined vaccines against diphtheria, tetanus and pertussis.
DERWENT CLASS: B04
INVENTOR(S): ARTOIS, C; DE HEYDER, K; DESMONS, P; GARCON, N; MAINIL, R; HEYDER, K D
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9948525	A1	19990930	(199949)*	EN	35
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9934172	A	19991018	(200009)		
NO 2000004758	A	20001108	(200067)		
BR 9909037	A	20001205	(200101)		
EP 1066053	A1	20010110	(200103)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI					
CN 1295481	A	20010516	(200146)		
AU 735619	B	20010712	(200147)		
CZ 2000003536	A3	20010815	(200157)		
HU 2001001323	A2	20010828	(200157)		

KR 2001034630	A	20010425	(200164)	
MX 2000009378	A1	20010301	(200170)	
JP 2002507581	W	20020312	(200220)	44
ZA 2000004956	A	20020227	(200223)	50
US 2003022304	A1	20030130	(200311)	
NZ 506604	A	20030228	(200323)	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9948525	A1		WO 1999-EP1959	19990322
AU 9934172	A		AU 1999-34172	19990322
NO 2000004758	A		WO 1999-EP1959	19990322
			NO 2000-4758	20000922
BR 9909037	A		BR 1999-9037	19990322
			WO 1999-EP1959	19990322
EP 1066053	A1		EP 1999-915692	19990322
			WO 1999-EP1959	19990322
CN 1295481	A		CN 1999-804445	19990322
AU 735619	B		AU 1999-34172	19990322
CZ 2000003536	A3		WO 1999-EP1959	19990322
			CZ 2000-3536	19990322
HU 2001001323	A2		WO 1999-EP1959	19990322
			HU 2001-1323	19990322
KR 2001034630	A		KR 2000-710518	20000922
MX 2000009378	A1		MX 2000-9378	20000925
JP 2002507581	W		WO 1999-EP1959	19990322
			JP 2000-537572	19990322
ZA 2000004956	A		ZA 2000-4956	20000918
US 2003022304	A1	Cont of	WO 1999-EP1959	19990322
		Cont of	US 2000-647032	20001031
			US 2002-217572	20020813
NZ 506604	A		NZ 1999-506604	19990322
			WO 1999-EP1959	19990322

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9934172	A	Based on	WO 9948525
BR 9909037	A	Based on	WO 9948525
EP 1066053	A1	Based on	WO 9948525
AU 735619	B	Previous Publ.	AU 9934172
		Based on	WO 9948525
CZ 2000003536	A3	Based on	WO 9948525
HU 2001001323	A2	Based on	WO 9948525
JP 2002507581	W	Based on	WO 9948525
NZ 506604	A	Based on	WO 9948525

PRIORITY APPLN. INFO: GB 1998-6456 19980325
AN 1999-580365 [49] WPIDS
AB WO 9948525 A UPAB: 19991124
NOVELTY - Reducing interference of a **capsular polysaccharide** component of a conjugated Haemophilus influenzae B vaccine (Hib) in a combined vaccine containing diphtheria and tetanus **toxoids** and acellular pertussis components (DTPa).

DETAILED DESCRIPTION - Reducing interference of a **capsular polysaccharide** component of a conjugated Haemophilus influenzae B vaccine (Hib) in a combined vaccine containing diphtheria and tetanus **toxoids** and acellular pertussis components (DTPa) comprises:

(a) pre-saturating **aluminum hydroxide** (AH) adjuvant with one or more selected antigens;

(b) selecting Hib and one or more additional antigens to be adsorbed on to **aluminum phosphate** (AP) adjuvant; and

(c) combining all the antigens.

An INDEPENDENT CLAIM is also included for a combined vaccine prepared this way.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Induction of specific immune responses.

USE - The method is used to prepare vaccines for preventing infection by diphtheria, tetanus, pertussis and H. influenzae, particularly in children.

ADVANTAGE - This method of vaccine preparation avoids interference from Hib while maintaining the maximum, stable activity of all antigens on their preferred adjuvant. Especially pertussis antigens are stably retained in their most potent form and Hib remians immunologically active for a long period. The method does not require addition of anions (contrast the method of WO 963722) and presaturation of AH means that the dose of potentially reactogenic AH can be reduced.

Dwg.0/0

L15 ANSWER 8 OF 18 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER:	1999-540273 [45] WPIDS
DOC. NO. NON-CPI:	N1999-400426
DOC. NO. CPI:	C1999-157763
TITLE:	Multivalent immunogenic molecule comprising carrier with T cell epitope and many carbohydrate fragments with B cell epitopes, particularly for vaccination against meningitis and diagnosis.
DERWENT CLASS:	B04 D16 S03
INVENTOR(S):	CHONG, P; KLEIN, M H; LINDBERG, A; KLEIN, M
PATENT ASSIGNEE(S):	(CONN-N) CONNAUGHT LAB LTD; (CHON-I) CHONG P; (KLEI-I) KLEIN M; (LIND-I) LINDBERG A
COUNTRY COUNT:	83

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9942130	A1	19990826	(199945)*	EN	82
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9926064	A	19990906	(200003)		
EP 1056470	A1	20001206	(200064)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
MX 2000008255	A1	20010301	(200170)		
BR 9908163	A	20011106	(200175)		

US 2001048929 A1 20011206 (200203)
JP 2002503705 W 20020205 (200212) 85
AU 754021 B 20021031 (200282)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9942130	A1	WO 1999-CA157	19990223
AU 9926064	A	AU 1999-26064	19990223
EP 1056470	A1	EP 1999-906002	19990223
		WO 1999-CA157	19990223
MX 2000008255	A1	MX 2000-8255	20000823
BR 9908163	A	BR 1999-8163	19990223
		WO 1999-CA157	19990223
US 2001048929	A1	US 1998-27956	19980223
JP 2002503705	W	WO 1999-CA157	19990223
		JP 2000-532144	19990223
AU 754021	B	AU 1999-26064	19990223

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9926064	A	Based on	WO 9942130
EP 1056470	A1	Based on	WO 9942130
BR 9908163	A	Based on	WO 9942130
JP 2002503705	W	Based on	WO 9942130
AU 754021	B	Previous Publ.	AU 9926064
		Based on	WO 9942130

PRIORITY APPLN. INFO: US 1998-27956 19980223
AN 1999-540273 [45] WPIDS
AB WO 9942130 A UPAB: 19991103
NOVELTY - Multivalent immunogenic molecule (I) comprises:
(i) carrier (Ia) having at least one functional T-cell epitope and
(ii) many different carbohydrate fragments (Ib), all linked to (Ia) and each having at least one functional B-cell epitope.
(Ia) increases the immunogenicity of (Ib).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) methods for preparing (I);
(2) immunogenic composition (A) for protection against meningitis comprising pneumococcal and **meningococcal** (I) and an immunogenic, synthetic PRP (3 beta -D-ribose-(1-1) ribosyl-5-phosphate)-peptide conjugate;
(3) methods for detecting (I); and
(4) diagnostic kits for detecting (I).
ACTIVITY - Antibacterial; antitumor.
MECHANISM OF ACTION - Induction of specific immune response.
Mice were immunized intramuscularly with 20 mu g (as oligosaccharide) of a conjugate of tetanus **toxoid** with oligosaccharides from the **capsular polysaccharides** of Streptococcus pneumoniae serotypes 6B, 14, 19F and 23F, formulated with 3 mg **aluminum phosphate**. Two further half-doses were given at 2 week intervals, then antisera collected. Reactive titers against 14 and 19F were 2-3 orders of

magnitude greater than for non-immunized controls, about 30 times higher for 23F but no significant response was observed against 6B.

USE - (I) are used to generate an immune response, specifically for protective vaccination against meningitis (Streptococcus pneumoniae or Neisseria **meningitidis**), but also against tumor-related antigens and antigens from other bacteria, e.g. Escherichia coli, Salmonella typhi, Streptococcus mutans, Cryptococcus neoformans, Klebsiella, Staphylococcus aureus or Pseudomonas aeruginosa; to detect, by complex formation, (I)-reactive antibodies and to raise (Ib)-specific antibodies, either for diagnostic detection of the corresponding antigen in usual immunoassays or, if directed against tumor antigens, for conjugation to anticancer agents.

ADVANTAGE - The combination of T- and B-cell epitopes in a single vaccine results in a strong and long-lasting humoral immunity.

Dwg.0/11

L15 ANSWER 9 OF 18 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1999-494397 [41] WPIDS
DOC. NO. CPI: C1999-144955
TITLE: Vaccine containing pneumococcal or **meningococcal** antigen, interleukin-12 and suspended mineral.
DERWENT CLASS: B04 D16
INVENTOR(S): ELDRIDGE, J H; LAPOSTA, V J
PATENT ASSIGNEE(S): (AMCY) AMERICAN CYANAMID CO
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9940936	A2	19990819	(199941)*	EN	82
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9925965	A	19990830	(200003)		
BR 9907884	A	20001024	(200058)		
EP 1053015	A2	20001122	(200061)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK NL PT RO SE SI					
CN 1292706	A	20010425	(200143)		
KR 2001040898	A	20010515	(200167)		
JP 2002502882	W	20020129	(200211)		70
MX 2000007879	A1	20011201	(200282)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9940936	A2	WO 1999-US2847	19990210
AU 9925965	A	AU 1999-25965	19990210
BR 9907884	A	BR 1999-7884	19990210
		WO 1999-US2847	19990210
EP 1053015	A2	EP 1999-905924	19990210

		WO 1999-US2847	19990210
CN 1292706	A	CN 1999-803879	19990210
KR 2001040898	A	KR 2000-708806	20000811
JP 2002502882	W	WO 1999-US2847	19990210
		JP 2000-531187	19990210
MX 2000007879	A1	MX 2000-7879	20000811

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9925965	A	Based on	WO 9940936
BR 9907884	A	Based on	WO 9940936
EP 1053015	A2	Based on	WO 9940936
JP 2002502882	W	Based on	WO 9940936

PRIORITY APPLN. INFO: US 1998-74528P 19980212
AN 1999-494397 [41] WPIDS
AB WO 9940936 A UPAB: 19991011
NOVELTY - Vaccine (A), or immunogenic composition (B), comprises a pneumococcal antigen (PAg) or **meningococcal** antigen (MAg); interleukin-12 (IL-12) and suspended mineral compound (I) as adjuvant, and optionally a vehicle.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Induction of a specific immune response. IL-12 modulates the immunoglobulin (Ig)G subclass response to the antigens, associated with a change in T-helper cell phenotype from Th2- to Th1-like.

USE - (A) are used to induce a protective immune response against pneumococci or **meningococci.**

ADVANTAGE - Formulation with IL-12 and (I) results in quantitatively or qualitatively better antibody and cell-mediated responses. Particularly the adjuvant increases the interferon-gamma response to vaccination and the proportion of complement-fixing antibodies (IgG2a and IgG2b). IL-12 also improves response to weakly immunogenic antigens and allows a reduction in the dose of toxic antigens required to induce an adequate response.

Dwg.0/0

L15 ANSWER 10 OF 18 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999210004 MEDLINE
DOCUMENT NUMBER: 99210004 PubMed ID: 10195629
TITLE: Haemophilus influenzae type b conjugate vaccine stability: catalytic depolymerization of PRP in the presence of **aluminum hydroxide.**
AUTHOR: Sturgess A W; Rush K; Charbonneau R J; Lee J I; West D J; Sitrin R D; Hennessy J P Jr
CORPORATE SOURCE: Bioprocess and Bioanalytical Research, Merck Research Laboratories, West Point, PA 19486, USA.
SOURCE: VACCINE, (1999 Mar 5) 17 (9-10) 1169-78.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990614
Last Updated on STN: 19990614

Entered Medline: 19990602

AB The structural stability of the Haemophilus influenzae type b (Hib) **capsular polysaccharide,** polyribosylribitolphosphate (PRP) in an **aluminum hydroxide** adsorbed, **polysaccharide**-protein conjugate vaccine was monitored using modifications of an HPLC assay developed by Tsai et al. [Tsai C-M, Gu X-X, Byrd RA. Quantification of **polysaccharide** in Haemophilus influenzae type b conjugate and **polysaccharide** vaccines by high-performance anion-exchange chromatography with pulsed amperometric detection. Vaccine 1993;12:700-706.]. As applied to products containing PRP conjugated to the **outer membrane protein** complex (OMPC) from Neisseria **meningitidis**, this assay allows direct measurement of the total PRP content in very complex samples including commercial vaccine products. In addition, with the use of a high-speed centrifugation step, the assay can be used to directly quantify any PRP that is not conjugated to the OMPC carrier protein. These results provide evidence of what appears to be a catalytic reaction taking place between the phosphodiester bond of PRP and the **aluminum hydroxide** adjuvant that results in hydrolysis of the PRP polymer into smaller chain lengths and liberation of PRP oligomers from the conjugate particle. The reaction approaches an asymptotic limit after approximately two years at 2-8 degrees C. Clinical studies which span this time period confirm that the modest decrease in conjugated PRP content over time does not impact the overall clinical effectiveness of PRP-OMPC-containing vaccines.

L15 ANSWER 11 OF 18 MEDLINE
ACCESSION NUMBER: 1998214909 MEDLINE
DOCUMENT NUMBER: 98214909 PubMed ID: 9554288
TITLE: Effect of **aluminium hydroxide** and **meningococcal** serogroup C **capsular polysaccharide** on the immunogenicity and reactogenicity of a group B Neisseria **meningitidis** outer membrane vesicle vaccine.
AUTHOR: Rosenqvist E; Hoiby E A; Bjune G; Aase A; Halstensen A; Lehmann A K; Paulssen J; Holst J; Michaelsen T E; Nokleby H; Froholm L O; Closs O
CORPORATE SOURCE: Department of Vaccinology, National Institute of Public Health, Oslo, Norway.
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1998) 92 323-33.
Journal code: 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625

AB Three different formulations of an outer membrane vesicle (OMV) vaccine against group B **meningococcal** disease have been prepared and tested for immunogenicity and reactogenicity in adult

volunteers. The vaccines were prepared with or without **aluminium hydroxide** and serogroup C-polysaccharide (C-ps). Doses from 12.5 to 100 micrograms protein were given twice at a six weeks' interval. All three formulations were well tolerated and highly immunogenic, inducing bactericidal and opsonizing antibodies in humans. Adsorption of OMVs to **aluminium hydroxide** reduced the pyrogenicity in rabbits. The differences in immunogenicity between the formulations were relatively small, but after the second dose a stronger booster response was observed when the vaccines were adsorbed. Thus, a formulation with OMVs and C-ps represents a safe and highly immunogenic vaccine, even without **aluminium hydroxide**.

L15 ANSWER 12 OF 18 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998040280 EMBASE
TITLE: **Meningococcal** vaccine development: A novel approach.
AUTHOR: Fusco P.C.; Blake M.S.; Michon F.
CORPORATE SOURCE: P.C. Fusco, North American Vaccine, Inc., 12103 Indian Creek Court, Beltsville, MD 20705, United States
SOURCE: Expert Opinion on Investigational Drugs, (1998) 7/2 (245-252).
Refs: 53
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Neisseria **meningitidis** is a major world-wide cause of meningitis. Effective **capsular polysaccharide** (**CPS**) vaccines, that elicit **CPS**-specific bactericidal (BC) antibodies, were previously developed and licensed to protect against **meningococcal** disease. However, due to their T-cell independent character, **CPS** vaccines are useless in infants and do not provide immunological memory or long-lasting protection in adults. **CPS**-protein conjugate vaccines are being developed to improve and broaden vaccine efficacy by creating T-cell dependent antigens. However, group B **meningococci** (GBM) are responsible for nearly half of **meningococcal** disease and possess a **CPS**, composed a polysialic acid, that is poorly immunogenic. N-propionyl (NPr) modification of the GBM **polysaccharide** (GBMP) has enhanced its immunogenicity, but BC antibodies are not induced at high levels, even when conjugated to conventional protein carriers, unless adjuvants stronger than **aluminium hydroxide** are used. We have chosen to couple the NPr-GBMP by reductive amination to a recombinant GBM class 3 porin (rPorB), which we have shown to modulate the immune response in animals towards the production of **CPS**-specific BC antibodies. We have also combined this conjugate with similar **CPS**-rPorB conjugates for groups A and C **meningococci** to form a trivalent A/B/C conjugate vaccine. This trivalent **meningococcal** vaccine has been shown to be safe and highly immunogenic in mice and non

human primates, generating **CPS**-specific BC antibodies for each of the 3 major serogroups, which should provide world-wide protection against **meningococcal** disease.

L15 ANSWER 13 OF 18 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 91366153 MEDLINE
DOCUMENT NUMBER: 91366153 PubMed ID: 1909736
TITLE: Human IgA1 blockade of IgG-initiated lysis of Neisseria **meningitidis** is a function of antigen-binding fragment binding to the **polysaccharide capsule.**
AUTHOR: Jarvis G A; Griffiss J M
CORPORATE SOURCE: Department of Laboratory Medicine, University of California, San Francisco.
CONTRACT NUMBER: AI21171 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1991 Sep 15) 147 (6) 1962-7. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911103
Last Updated on STN: 19911103
Entered Medline: 19911017

AB We have recently shown that human IgA1 can initiate lysis of group C Neisseria **meningitidis** via the classical C pathway when bound to specific **outer membrane proteins**, but that IgA1 can also function as a blocking antibody when bound to the **polysaccharide capsule** of **meningococci**. In this report, we further characterized IgA1 blockade by examining the effect of IgA1 on IgG-initiated immune lysis of group C **meningococci**. We purified IgG and monomeric IgA1 from either convalescent group C **meningococcal** case sera or tetravalent (A, C, Y, W135) **polysaccharide** vaccinate sera. In the absence of IgA1, IgG initiated complete lysis (greater than 99%) of strains 118V (C:P3,4:L2,4) 126E (C:P3:L1,8), and 35E (C:P5:L2). Addition of IgA1 to the bactericidal reaction mixture completely blocked the lytic function of IgG. Removal of the Fc portion of IgA1 with either pepsin or IgA1 protease did not affect blockade. Both the F(ab')2 and Fab derivatives of IgA1 blocked lysis quantitatively as well as intact IgA1. The Fc fragment produced by IgA1 protease cleavage neither increased nor decreased Fab-mediated blockade. IgA1 and its Fab and F(ab')2 fragments blocked IgG-initiated lysis via either the classical pathway in factor B-depleted and in properdin-deficient serum, the alternative pathway in MgEGTA-chelated serum, or both pathways combined. Absorption of the IgA1 and IgG with **alum** -bound group C **polysaccharide** completely removed blocking and lytic activity, respectively, indicating that both the blocking IgA1 and the lytic IgG were specific for the group C **capsule** . Blocking by IgA1 was a linear function of the **polysaccharide** Ag-binding capacity (ABC) ratio of blocking IgA1 to lytic IgG. Complete blockade was observed at an ABC ratio of 5.5. At ABC ratios of 3.3 and 4.4, IgA1 affected significant blockade whether added previous to, concurrent with, or subsequent to sensitization of the organisms with IgG. With the use of a C **polysaccharide** ELISA, we found that the binding of IgA1 to

the group C **capsule** in the presence of IgG exhibited positive cooperativity and therefore that blockade was independent of the ability of IgA1 to directly compete with IgG for binding to epitopes within the group C **capsule**. We conclude that IgA1, when bound to the group C **polysaccharide capsule**, can block IgG-initiated lysis of group C **meningococci** through either the classical or the alternative pathway before or after the organism is exposed to IgG, and that blockade is an Fc-independent event.

L15 ANSWER 14 OF 18 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 91181308 MEDLINE
DOCUMENT NUMBER: 91181308 PubMed ID: 1901187
TITLE: Immunogenicity in adult males of a Neisseria **meningitidis** group B vaccine composed of polysaccharide complexed with **outer membrane proteins**.
AUTHOR: Lifely M R; Roberts S C; Shepherd W M; Esdaile J; Wang Z; Cleverly A; Aulaqi A A; Moreno C
CORPORATE SOURCE: Department of Experimental Immunobiology, Wellcome Biotech, Beckenham, Kent, UK.
SOURCE: VACCINE, (1991 Jan) 9 (1) 60-6.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910519
Last Updated on STN: 19980206
Entered Medline: 19910501

AB Twenty five adult male volunteers were given a vaccine composed of the **capsular** B **polysaccharide** non-covalently complexed to serotype 6 **outer membrane proteins** (**OMP**) of Neisseria **meningitidis**. Subjects were divided into three dose groups receiving 50, 100 or 150 micrograms vaccine in **aluminium hydroxide** in each of three injections spaced 4 weeks apart. Systemic signs/symptoms considered clinically significant were recorded on 6% (4/70) of occasions and were succeeded by withdrawal of two volunteers from the study. Local injection site reactions, mostly mild to moderate, were reported after all vaccinations with one such reaction leading to a third volunteer withdrawing from the study. Geometric mean anti-B responses before immunization and 1 week after the third immunization (9 weeks) were 3.60 and 7.12 micrograms ml-1 in the 50 micrograms group (p less than 0.05) 2.05 and 12.19 micrograms ml-1 in the 100 micrograms group (p less than 0.001), and 3.68 and 14.20 micrograms ml-1 in the 150 micrograms group (p less than 0.001). The anti-B response was predominantly of the IgM isotype and persistence above prevaccination levels was evident for at least 12 months. Anti-type 6 **OMP** responses were also evidenced with geometric mean multiplicative increases over prevaccination levels at 9 weeks and 6 months of 7.8 and 4.2 for the 50 micrograms group, 11.6 and 5.6 for the 100 micrograms group and 6.8 and 3.4 for the 150 micrograms group. The bulk of this response was of the IgG isotype. Passive protection of mice was achieved with

both pre- and post-vaccination (9 weeks; 100 and 150 micrograms groups) pools of sera.(ABSTRACT TRUNCATED AT 250 WORDS)

L15 ANSWER 15 OF 18 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 86283798 MEDLINE
DOCUMENT NUMBER: 86283798 PubMed ID: 2874327
TITLE: Immunogenicity in infants of Haemophilus influenzae type B polysaccharide in a conjugate vaccine with Neisseria **meningitidis outer-membrane protein.**
AUTHOR: Einhorn M S; Weinberg G A; Anderson E L; Granoff P D; Granoff D M
CONTRACT NUMBER: RO1 AI 17962 (NIAID)
RR-36 (NCRR)
T32 AI 07172 (NIAID)
SOURCE: LANCET, (1986 Aug 9) 2 (8502) 299-302.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198609
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860917

AB 63 children, aged 2-17 months, were given a new conjugate vaccine composed of the **capsular polysaccharide** of Haemophilus influenzae type b linked to a Neisseria **meningitidis outer-membrane protein.** Subjects under 7 months received two injections separated by 1 month, and older subjects received either one or two injections. There were no systemic reactions to this vaccine when it was given with **aluminium hydroxide.** A single injection of vaccine was highly immunogenic; the geometric mean serum anticapsular antibody concentrations before immunisation and 1 month later were 0.35 microgram/ml and 0.98 microgram/ml for babies of 2-3 months, 0.12 microgram/ml and 1.85 micrograms/ml for those of 4-6 months, and 0.15 microgram/ml and 4.1 micrograms/ml for those of 8-17 months (p less than or equal to 0.003 for each age group). After a second injection of vaccine, 80% and 76% of infants of 2-3 and 4-6 months, respectively, had antibody concentrations greater than 1.0 micrograms/ml. Most subjects showed evidence of IgG responses as measured by enzyme-linked immunosorbent assay. 6-12 months after immunisation, serum antibody levels had fallen (p less than 0.05) but they remained higher than those of unimmunized controls (p less than 0.001).

L15 ANSWER 16 OF 18 TOXCENTER COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:912 TOXCENTER
COPYRIGHT: Copyright 2003 ASHP
DOCUMENT NUMBER: 24-01375
TITLE: Immunogenicity in infants of Haemophilus influenzae type b polysaccharide in a conjugate vaccine with Neisseria **meningitidis outer-membrane protein**
AUTHOR(S): Einhorn, M. S.; Weinberg, G. A.; Anderson, E. L.; Granoff, P. D.; Granoff, D. M.
CORPORATE SOURCE: Div. of Infectious Diseases, St. Louis Children's

Hosp., P.O. Box 14871, St. Louis, MO 63178
SOURCE: Lancet (England), (Aug 9 1986) Vol. 2, pp. 299-302. 23 Refs
CODEN: LANCAO. ISSN: 0023-7507.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 86:2357
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20011116

AB To determine the safety and immunogenicity of a conjugate vaccine composed of **capsular polysaccharide** of H. influenzae type b linked to a N. **meningitidis** group B **outer-membrane protein**, reconstituted with and without **aluminum hydroxide** in 63 children (aged 2-17 months), children under 7 months received 2 injections separated by one month, and older children received either one or 2 injections. There were no systemic reactions to the vaccine when given with **aluminum hydroxide** due to slower release of the vaccine adsorbed to the **aluminum hydroxide**. A single injection of vaccine was highly immunogenic; the geometric mean serum anticapsular antibody concentrations before immunization and one month later were 0.35 mcg/ml and 0.98 mcg/ml for infants of 2-3 months, 0.12 mcg/ml and 1.85 mcg/ml for those of 4-6 months, and 0.15 mcg/ml and 4.1 mcg/ml for those of 8-17 months. After a second injection of vaccine, 80% and 76% of infants 2-3 and 4-6 months, respectively, had antibody concentration of >1.0 mcg/ml. Most subjects showed evidence of IgG responses as measured by ELISA. Six to 12 months after immunization, serum antibody levels had fallen but remained higher than those of unimmunized controls. It was concluded that the antibody elicited by the vaccine is biologically active and that the antigenic activity of the polysaccharide was preserved during coupling to the protein.
Elvira deC. Weiss

L15 ANSWER 17 OF 18 MEDLINE
ACCESSION NUMBER: 86301534 MEDLINE
DOCUMENT NUMBER: 86301534 PubMed ID: 3091433
TITLE: Class 1/3 **outer membrane protein** vaccine against group B, type 15, subtype 16 **meningococci**.
AUTHOR: Poolman J T; Beuvery E C; Hopman C T; Witvliet M H; Timmermans H A; Teerlink T; Zanen H C
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1986) 63 147-52.
Journal code: 0427140. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19861021

AB Neisseria **meningitidis capsular polysaccharides** and **outer membrane proteins** have been incorporated in vaccines and the

potential of these vaccines has been evaluated in man. **Polysaccharides** are the most attractive candidates for a vaccine against group A and C **meningococci** whereas **outer membrane proteins** may have a potential for a vaccine against group B **meningococci**. This paper describes the characteristics of the five classes of **outer membrane proteins** of group B **meningococci** and the protective (bactericidal) activity of monoclonal antibodies against class 1 and 2 or 3 **outer membrane proteins**. Monoclonal antibodies against class 1 **outer membrane proteins** were bactericidal irrespective of the growth conditions of the bacterium. On the other hand, these conditions influenced the bactericidal activity of monoclonal antibodies against class 2 or 3 **outer membrane proteins**. These data indicate that class 1 **outer membrane protein** is an attractive component of a vaccine. The Blake and Gotschlich procedure for the isolation of gonococcal **outer membrane protein** II (1) was adapted for the isolation of a combination of class 1 and 3 **outer membrane proteins** from group B, type 15 **meningococci**. The combination of both **outer membrane proteins** was adsorbed to **ALPO4** in the presence of the detergent Zwittergent 3-14. The vaccine was injected into mice. The antibodies were strongly bactericidal and Western blot analysis indicated that both **outer membrane proteins** induced antibodies. The vaccine may have a potential to combat an epidemic caused by group B, type 15 **meningococci**. Such an epidemic was observed in some N.W. - European countries.

L15 ANSWER 18 OF 18 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 85053438 MEDLINE
DOCUMENT NUMBER: 85053438 PubMed ID: 6437983
TITLE: Development of a Neisseria **meningitidis** group B serotype 2b protein vaccine and evaluation in a mouse model.
AUTHOR: Wang L Y; Frasch C E
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AB Although serotype 2 remains the predominant cause of group B Neisseria **meningitidis** disease in many parts of the world, most cases of this disease are now due to serotype 2b rather than 2a. For this reason, we adapted the serotype 2a vaccine method of C. E. Frasch and M. S. Peppler (Infect. Immun. 37:271-280, 1982) to the production of a serotype 2b protein vaccine. A spontaneously occurring nonencapsulated mutant of the group B serotype 2b strain 3006 was obtained by selection on group B antiserum agar. Serotype 2b **outer membrane protein** vaccines were prepared with less than 1% lipoplysaccharide contamination. The

immunogenicity of these vaccines was evaluated in mice in the presence and absence of **meningococcal** group B and group C **capsular polysaccharides**. The group B and group C **polysaccharides** equally potentiated the antibody response to the serotype 2b protein. Addition of **aluminum hydroxide** or **aluminum phosphate** markedly improved the antibody response to the serotype 2b protein, but **aluminum hydroxide**-adjuvanted vaccines consistently elicited higher antibody levels. **Aluminum hydroxide**-adsorbed serotype 2a and 2b protein vaccines were evaluated for induction of cross-protective bactericidal antibodies. The 2a vaccines were 2a specific, whereas the 2b vaccines elicited antibodies strongly bactericidal for both 2a and 2b **meningococcal** strains and protected against bacteremia in a mouse model. It may therefore be possible to provide protection against both 2a and 2b disease by using an **aluminum hydroxide**-adsorbed protein vaccine containing a single serotype 2 protein component.

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L16 4699 SEA FILE=MEDLINE ABB=ON PLU=ON "NEISSERIA MENINGITIDIS"/CT

L17 1929 SEA FILE=MEDLINE ABB=ON PLU=ON "ALUMINUM HYDROXIDE"/CT

L18 441 SEA FILE=MEDLINE ABB=ON PLU=ON "ALUM COMPOUNDS"/CT

L19 12 SEA FILE=MEDLINE ABB=ON PLU=ON L16 AND (L17 OR L18)

L19 ANSWER 1 OF 12 MEDLINE

AN 2002302438 MEDLINE

TI [Evaluation of the immunological activity and safety of group B meningococcal vaccine prepared from a natural complex of specific polysaccharide and outer membrane proteins].
Otsenka immunologicheskoi aktivnosti i bezopasnosti meningokokkovoi gruppy B vaktsiny iz prirodnogo kompleksa spetsificheskogo polisakharida i belkov naruzhnoi membrany.

AU Kuvakina V I; Golovina L I; Mishina A I; Skirda T A; Bobyleva G V; Mikheeva N G; Chernyshova T F; Temper R M; Ermolenko Z N

SO ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, (2002 Mar-Apr) (2) 33-7.
Journal code: 0415217. ISSN: 0372-9311.

AB Immunological activity and safety of group B meningococcal vaccine prepared from a natural complex of specific polysaccharide and outer membrane proteins were under study. The immunological safety of the vaccine was evaluated by the absence of antibodies to denaturated and native DNA (d-DNA and n-DNA). As shown with the use of the enzyme immunoassay (EIA), the administration of the vaccine did not induce antibody formation to d-DNA and n-DNA during the observation period. The titer of bactericidal antibodies in the immune bacteriolysis assay (IBA) to the vaccine strain B:2b:P1.2 after immunization increased four-fold and greater in 80% of the vaccinated persons. The significant increase of bactericidal antibodies to heterologous strains B:2a:P1.2 and B:15:P1.7 was registered in 20-30% of the vaccinees, respectively. A month after the repeated vaccination an increase in specific IgG antibodies to the complex antigen was found to occur according to EIA results. The use of RIB made it possible to evaluate the preventive activity of group B meningococcal vaccine as a whole and to suppose that the vaccine induced mainly type-specific response.

L19 ANSWER 2 OF 12 MEDLINE
AN 2001371340 MEDLINE
TI Immunization with recombinant Opc outer membrane protein from Neisseria meningitidis: influence of sequence variation and levels of expression on the bactericidal immune response against meningococci.
AU Jolley K A; Appleby L; Wright J C; Christodoulides M; Heckels J E
SO INFECTION AND IMMUNITY, (2001 Jun) 69 (6) 3809-16.
Journal code: 0246127. ISSN: 0019-9567.
AB The opc gene from Neisseria meningitidis was cloned into the pRSETA vector, and recombinant protein was expressed at high levels in Escherichia coli. The protein was readily purified by affinity chromatography and used for immunization with conventional Al(OH)3 adjuvant or after incorporation into liposomes and Zwittergent micelles. The resulting sera were analyzed for their ability to recognize purified recombinant protein and "native" protein in an enzyme immunoassay with outer membranes and by whole-cell immunofluorescence. Immunization with Al(OH)3 induced high levels of antibodies which reacted with the purified protein but did not recognize whole cells. In contrast, liposomes and micelles induced antibodies which reacted with the native protein in whole cells. The addition of monophosphoryl lipid A (MPLA) to either liposomes or micelle preparations increased the magnitude of the immune response and induced a wider range of immunoglobulin subclasses. This was associated with the ability of the sera to induce complement-mediated killing of the homologous strain. The most effective bactericidal activity was observed with Opc protein incorporated into liposomes containing MPLA. The magnitude of the bactericidal effect was strongly influenced by the level of expression of the Opc protein and was abolished by limited variation in the sequence of the protein expressed by heterologous strains.

L19 ANSWER 3 OF 12 MEDLINE
AN 1999180526 MEDLINE
TI Preformulation study of the vaccine candidate P64k against Neisseria meningitidis.
AU Exposito Raya N; Mestre Luaces M; Silva Rodriguez R; Nazabal Galvez C; Pena Rivero M; Martinez de la Puente N; Font Batista M; Guillen Nieto G
SO BIOTECHNOLOGY AND APPLIED BIOCHEMISTRY, (1999 Apr) 29 (Pt 2) 113-7.
Journal code: 8609465. ISSN: 0885-4513.
AB We have previously isolated, cloned and expressed in Escherichia coli the lpdA gene coding for a high-molecular-mass protein (P64k) common to many meningococcal strains. P64k is an outer membrane lipoamide dehydrogenase that is highly immunogenic in animals. Here we describe a preformulation study of the recombinant protein as a vaccine candidate against Neisseria meningitidis, in which six variants containing the candidate were tested. Three assays were used to identify the most suitable variant for further evaluation: percentage of adsorption, identification of P64k by SDS/PAGE, and immunogenicity in mice. All the preformulation variants studied showed more than 98% of adsorption of P64k on the aluminium gel. After desorption, P64k was also identified by SDS/PAGE in the six preformulation variants. Seroconversion was attained in all groups analysed. On the basis of these results, the most effective variant consisted of 20 microg/ml P64k plus 0.5 mg/ml aluminium hydroxide.

L19 ANSWER 4 OF 12 MEDLINE
AN 1998214909 MEDLINE
TI Effect of aluminium hydroxide and meningococcal serogroup C capsular polysaccharide on the immunogenicity and reactogenicity of a group B Neisseria meningitidis outer membrane vesicle vaccine.
AU Rosenqvist E; Hoiby E A; Bjune G; Aase A; Halstensen A; Lehmann A K; Paulssen J; Holst J; Michaelsen T E; Nokleby H; Froholm L O; Closs O
SO DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1998) 92 323-33. Journal code: 0427140. ISSN: 0301-5149.
AB Three different formulations of an outer membrane vesicle (OMV) vaccine against group B meningococcal disease have been prepared and tested for immunogenicity and reactogenicity in adult volunteers. The vaccines were prepared with or without aluminium hydroxide and serogroup C-polysaccharide (C-ps). Doses from 12.5 to 100 micrograms protein were given twice at a six weeks' interval. All three formulations were well tolerated and highly immunogenic, inducing bactericidal and opsonizing antibodies in humans. Adsorption of OMVs to aluminium hydroxide reduced the pyrogenicity in rabbits. The differences in immunogenicity between the formulations were relatively small, but after the second dose a stronger booster response was observed when the vaccines were adsorbed. Thus, a formulation with OMVs and C-ps represents a safe and highly immunogenic vaccine, even without aluminium hydroxide.

L19 ANSWER 5 OF 12 MEDLINE
AN 1998173514 MEDLINE
TI Bactericidal activity of antibodies elicited against the Neisseria meningitidis 37-kDa ferric binding protein (FbpA) with different adjuvants.
AU Gomez J A; Criado M T; Ferreiros C M
SO FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, (1998 Jan) 20 (1) 79-86. Journal code: 9315554. ISSN: 0928-8244.
AB The 37-kDa ferric binding protein, FbpA, from three Neisseria meningitidis strains was purified to homogeneity with iron-affinity chromatography and used for immunisation of mice employing four different adjuvants: aluminium hydroxide, Freund's, the saponin Quil-A, and a Ribi adjuvant system (RAS). Controls immunised without adjuvant were also included. All sera obtained were monospecific for the meningococcal FbpA, with antibody titres higher when RAS and Quil-A were used (256), PBS resulting in titres similar to those of Freund's (64), and, surprisingly, with no antibodies elicited when aluminium hydroxide, the only approved adjuvant for use in humans, was used. All anti-FbpA sera bound to intact meningococcal cells, showing a complete cross-reactivity, but the bactericidal activity of anti-FbpA antibodies, demonstrated for the first time in this work, was low (32% of killing with the homologous strain), and the analysis of immunoglobulin isotypes showed that the non-bactericidal IgG1 was predominant. The results confirm that the FbpA is surface-exposed, antigenic, and able to elicit bactericidal antibodies, although, in the conditions and with the adjuvants tested, killing efficacy was low and cross-killing was very variable, not supporting the inclusion of this protein in vaccine formulations. Nevertheless, given the high conservation of the FbpA in the genus Neisseria, its surface exposure and its antigenicity, studies on immunisation with peptides corresponding to the exposed epitopes and/or new adjuvant systems could improve the bactericidal response to this protein, making it suitable for vaccine development.

L19 ANSWER 6 OF 12 MEDLINE
AN 94337552 MEDLINE
TI [The effect of detergents on the immunological activity of the antigens of Neisseria meningitidis serogroup B[].
Vliianie detergentov na immunologicheskuiu aktivnost' antigenov Neisseria meningitidis serogruppy B.
AU Bugaev L V; Shkurina E A; Karabak V I; Alliluev A P; Petrov A B
SO ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, (1993 Mar-Apr) (2) 11-5.
Journal code: 0415217. ISSN: 0372-9311.
AB The complex study of the influence of detergents of different classes and aluminum hydroxide, a traditional adjuvant, on the immunological activity of individual N. meningitidis antigens (outer membrane proteins, polysaccharide B) and the complex preparation containing all these antigens revealed that changes in the antigenic and immunogenic properties of the antigens under study depended on the degree of their purification and the character of modifying substances. Aluminum hydroxide proved to be the most active adjuvant: it stimulated immune response to both outer membrane proteins and antigens of the protein-polysaccharide complex, while decreasing the antigenicity of outer membrane proteins and polysaccharide. Detergents increased the antigenicity of outer membrane proteins, both purified and, to a lesser extent, contained in the complex; still the immune response only to the purified preparation could be stimulated.

L19 ANSWER 7 OF 12 MEDLINE
AN 91315786 MEDLINE
TI Immunization against serogroup B meningococci. Opsonin response in vaccinees as measured by chemiluminescence.
AU Lehmann A K; Halstensen A; Naess A; Vollset S E; Sjursen H; Bjune G
SO APMIS, (1991 Aug) 99 (8) 769-72.
Journal code: 8803400. ISSN: 0903-4641.
AB One hundred and thirteen healthy volunteers were immunized twice (six weeks apart) with four different doses (12.5, 25, 50 and 100 micrograms, measured as protein content) of an outer membrane vesicle vaccine from a serogroup B meningococcal strain (44/76, B:15:P1.16) complexed to serogroup C meningococcal polysaccharide and/or Al(OH)3 i.e. 12 different vaccines. Serum opsonic activity against the serogroup B strain was measured using a chemiluminescence method. A significant rise in serum opsonic activity was demonstrated in 84 volunteers (74%) six weeks after the first injection and in 97 (86%) six weeks after the second. All vaccinees with low preimmunization values (less than 25 mVs) experienced a significant increase in opsonic activity. A dose-related response was most evident for the vaccines containing adjuvant, and these vaccines were associated with a maximum response six weeks after the second injection, while the vaccines without Al(OH)3 induced a peak response six weeks after the first injection. The postimmunization opsonic activity was similar to that found in convalescent sera, indicating that the vaccines may protect against serogroup B meningococcal disease.

L19 ANSWER 8 OF 12 MEDLINE
AN 91272707 MEDLINE
TI [The sorption of a protein-polysaccharide complex isolated from Neisseria meningitidis serogroup B on aluminum hydroxide gels and

the immunological activity of the sorbed preparations].
Sorbtsiia belkovo-polisakharidnogo kompleksa, vydelennogo iz Neisseria meningitidis serogruppy B, na geli gidroksida aliumin immunologicheskaia aktivnost' sorbirovannykh preparatov.
AU Bugaev L V; Vartanian Iu P; Karabak V I; Kil'diushevskaia T V; Kuvakina V I; Basnak'ian I A; Alliluev A P; Machul'skaia K V; Borovkova V M; Petrov A B
SO ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, (1990 Nov) (11) 50-6.
Journal code: 0415217. ISSN: 0372-9311.
AB The protein-polysaccharide complex, isolated from group B N. meningitidis, is a variant of vaccine for the prophylaxis of group B N. meningitidis infection. In this investigation the influence of the complex of the physical properties of aluminium hydroxide gels, the amount of gel, pH and the duration of sorption on the process of sorption has been studied. Aluminium hydroxide has been shown to produce a stimulating effect on the response of mice to the polysaccharide and protein contained in the complex after immunization made in two injections. Gels with a smaller particle size have been found to possess greater adjuvant activity, as well as greater absorbing activity. The immunological activity of the complex, adsorbed ex tempore, has proved to be no different from that of the complex adsorbed in an hour.

L19 ANSWER 9 OF 12 MEDLINE
AN 89389589 MEDLINE
TI [The protective activity of the detoxified lipopolysaccharide of Neisseria meningitidis serogroup A in in vivo experiments].
Protektivnaia aktivnost' detoksitsirovannogo lipopolisakharida Neisseria meningitidis serogruppy A v opytakh in vivo.
AU Del'vig A A; Krasnoproshina L I; Bobyleva G V; Kuvakina V I
SO ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII, (1989 May) (5) 69-73.
Journal code: 0415217. ISSN: 0372-9311.
AB The immunogenic potency, toxicity, homologous and heterologous protective activity of lipopolysaccharide preparations obtained from serogroup A N. meningitidis (LPS A) were studied in animal experiments. These preparations were shown to possess very high protective activity. The alkaline treatment of native LPS A decreased the toxicity of the preparation almost 20 times and did not affect its immunogenic potency. Detoxified LPS A was capable of protecting mice from fatal meningococcemia resulting from infection with N. meningitidis strains, serogroups A, B and C; the adsorption of the preparation on aluminium hydroxide did not affect its protective activity. In view of the properties of detoxified LPS A revealed in this investigation, it may be regarded as a possible vaccinal preparation.

L19 ANSWER 10 OF 12 MEDLINE
AN 89009974 MEDLINE
TI Antibody response of adults to an aluminum hydroxide-adsorbed Neisseria meningitidis serotype 2b protein-group B polysaccharide vaccine.
AU Frasch C E; Zahradnik J M; Wang L Y; Mocca L F; Tsai C M
SO JOURNAL OF INFECTIOUS DISEASES, (1988 Oct) 158 (4) 710-8.
Journal code: 0413675. ISSN: 0022-1899.
AB A group B Neisseria meningitidis serotype protein vaccine was studied clinically in adults. The vaccine comprised

lipopolysaccharide-depleted outer membrane vesicles from a serotype 2b strain, 3006-M2, noncovalently complexed with group B meningococcal polysaccharide. Volunteers received 25 micrograms each of protein and polysaccharide administered intramuscularly either in 0.9% NaCl or adsorbed onto aluminum hydroxide on weeks 0 and 6. Most individuals experienced mild local reactions, but there were no systemic reactions. Both vaccine formulations stimulated antibodies to the outer membrane proteins of serotypes 2a:P1.2 and 2b:P1.2, but higher levels were achieved with the aluminum hydroxide-adsorbed vaccine after two immunizations. Vaccine-induced antibodies were primarily IgG and were bactericidal for both a serotype 2a and a serotype 2b strain. Induction of bactericidal antibodies has been shown to be a major predictor of protection against meningococcal disease.

L19 ANSWER 11 OF 12 MEDLINE
AN 86283798 MEDLINE
TI Immunogenicity in infants of Haemophilus influenzae type B polysaccharide in a conjugate vaccine with Neisseria meningitidis outer-membrane protein.
AU Einhorn M S; Weinberg G A; Anderson E L; Granoff P D; Granoff D M
SO LANCET, (1986 Aug 9) 2 (8502) 299-302.
Journal code: 2985213R. ISSN: 0140-6736.
AB 63 children, aged 2-17 months, were given a new conjugate vaccine composed of the capsular polysaccharide of Haemophilus influenzae type b linked to a Neisseria meningitidis outer-membrane protein. Subjects under 7 months received two injections separated by 1 month, and older subjects received either one or two injections. There were no systemic reactions to this vaccine when it was given with aluminium hydroxide. A single injection of vaccine was highly immunogenic; the geometric mean serum anticapsular antibody concentrations before immunisation and 1 month later were 0.35 microgram/ml and 0.98 microgram/ml for babies of 2-3 months, 0.12 microgram/ml and 1.85 micrograms/ml for those of 4-6 months, and 0.15 microgram/ml and 4.1 micrograms/ml for those of 8-17 months (p less than or equal to 0.003 for each age group). After a second injection of vaccine, 80% and 76% of infants of 2-3 and 4-6 months, respectively, had antibody concentrations greater than 1.0 micrograms/ml. Most subjects showed evidence of IgG responses as measured by enzyme-linked immunosorbent assay. 6-12 months after immunisation, serum antibody levels had fallen (p less than 0.05) but they remained higher than those of unimmunized controls (p less than 0.001).

L19 ANSWER 12 OF 12 MEDLINE
AN 85053438 MEDLINE
TI Development of a Neisseria meningitidis group B serotype 2b protein vaccine and evaluation in a mouse model.
AU Wang L Y; Frasch C E
SO INFECTION AND IMMUNITY, (1984 Nov) 46 (2) 408-14.
Journal code: 0246127. ISSN: 0019-9567.
AB Although serotype 2 remains the predominant cause of group B Neisseria meningitidis disease in many parts of the world, most cases of this disease are now due to serotype 2b rather than 2a. For this reason, we adapted the serotype 2a vaccine method of C. E. Frasch and M. S. Peppler (Infect. Immun. 37:271-280, 1982) to the production of a serotype 2b protein vaccine. A spontaneously occurring nonencapsulated mutant of the group B serotype 2b strain

capsular polysaccharides from Neisseria **meningitidis** serogroups A, C, W-135, and Y are chem. activated and selectively attached to a carrier protein by a covalent chem. bond, forming **polysaccharide**-protein conjugates capable of eliciting long-lasting immunity to a variety of N. **meningitidis** strains in children as well as adults.

L21 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 1999:244677 HCAPLUS
DOCUMENT NUMBER: 130:266367
TITLE: Selective and restricted depolymerization of microbial polysaccharides for preparation of conjugate vaccines
INVENTOR(S): **Ryall, Robert P.**
PATENT ASSIGNEE(S): Connaught Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
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PATENT INFORMATION:

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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5965714	A	19991012	US 1997-942852	19971002
CA 2305620	AA	19990415	CA 1998-2305620	19980929
AU 9896776	A1	19990427	AU 1998-96776	19980929
EP 1019437	A1	20000719	EP 1998-950831	19980929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-942852 A 19971002
WO 1998-US20625 W 19980929

AB The author discloses methods for the covalent attachment of poly- and oligosaccharides to proteins. In one example of the method, hydrogen peroxide is used to effect restricted hydrolysis of **capsular polysaccharide** (e.g., Streptococcus pneumoniae 19F). Following hydrolysis, the depolymd. polysaccharide is derivatized with adipic dihydrazide and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide and conjugated to diphtheria toxoid.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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